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The Potential Role of 5-Methyl-2 (3H)-Furanone in *Tamarindus indica* as Lipoxygenase (LOX) Inhibitor: in Silico Study

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Abstract. *Tamarindus indica* is the Fabaceae family that is used in the pharmaceutical theuraphic because it contains polyphenols. One of the studies is to have anti-inflammatory properties. When inflammation occurs, , the lipoxygenase (LOX) pathway will be formed as a mediator of acute inflammation. Reducing inflammation, it is necessary to control genes that play a role in increasing inflammation, one of which is LOX. This study aims to analyze the potential of the 5-Methyl-2 (3H)-Furanone compound on LOX action. The compound 5-Methyl-2 (3H) -Furanone (CID 11559) was downloaded from the PubChem database. The 5-LOX protein was downloaded from Protein Data Bank (PDB 6N2W) and and prepared by removing ligands and molecules that bind to Discovery Studio V19.1.0.18287. The compounds and proteins were interacted with the Vina autodock software integrated in the PyRX software and analyzed using Discovery Studio V19.1.0.18287. The results showed 5-Methyl-2 (3H) -Furanone binds to lipoxygenase on the active sites of Gln329, Arg518, Ile330, Leu153, Glu146, Asn328, and Asp290. The three bioactive compounds tamarin bind to lipoxygenase with hydrogen, hydrophobic and van der Waals forces. The ligands and proteins that are formed produce energy -6Kcal/mol. The interactions that occur between compounds contained in *Tamarindus indica* have potential as inhibitors of LOX and are predicted to be used as compounds for inflammatory therapy.

Keywords: Anti-inflammation, inhibitor, lipoxygenase, polyphenol, *Tamarindus indica*

INTRODUCTION

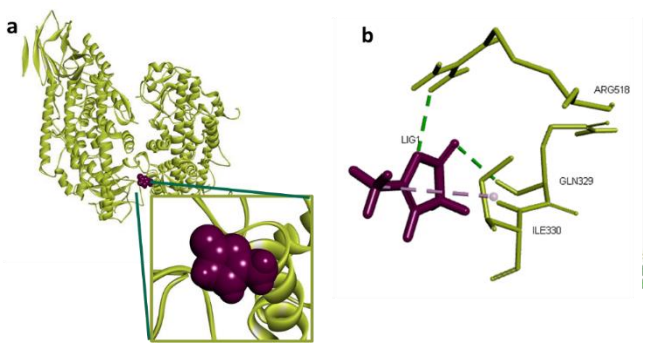
Inflammation showed that has different protein production in humans body (Bare et al., 2018). These condition has effect to human body. When inflammation occurs, the lipoxygenase (LOX) pathway will be formed as a mediator of acute inflammation. Reducing inflammation is necessary to control genes that play a role in increasing inflammation. One of enzyme that oxidizes arachidonic acid that has function to produce leukotriene (LTs). LTs has role as inflammation indicator in cells. One of the mechanism of the inflammatory mechanism is arachidonic acid which converted into LTs by lipoxygenase. In other way arachidonic converted to PGH2 by Cycloxygenase-2. Therefore, LOX and COX become target proteins in drug development as anti-inflammatory. The use of plants in traditional medicine is one of the solution to curve problem. *Tamarindus indica* is the Fabaceae family that is used in the pharmaceutical theuraphic because it contains polyphenols. One of the studies is to have anti-inflammatory properties. Recent research analyzed ethnopharmacology of *Tamarindus indica* and showed differences in the ways tamarind is used in local medicine in Africa (Havinga et al., 2010; Saideswara Rao & Mary Mathew, 2012). *Tamarindus indica* contains 5-Methyl-2 (3H) -Furanone around 10.61pp which reported as one of the chemicals compound that has theuraphic properties (Zhang et al., 1990). This study aims to analyze the potential of the 5-Methyl-2 (3H)-Furanone compound on LOX action.

MATERIALS AND METHOD

The compound 5-Methyl-2 (3H) -Furanone (CID 11559) file was downloaded from the PubChem database. The 5-LOX protein file was obtained from PDB (6N2W) and prepared by removing ligands and molecules that bind to Discovery Studio V19.1.0.18287. The compound and protein were interacted with the Vina autodock software integrated in the PyRX software and analyzed using Discovery Studio V19.1.0.18287

RESULTS AND DISCUSSION

5-Methyl-2 (3H) -Furanone is a bioactive compound contained in tamarine. Crude extract of tamarine has been reported to have an anti-inflammatory properties. In this study, tamarin was screened as an anti-inflammatory to inhibit lipoxygenase activity.



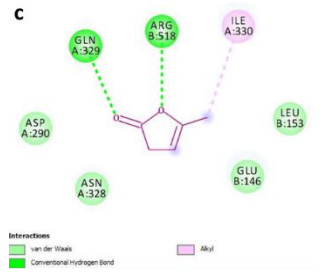


Figure 1. Interaction between Lipoxygenase and 5-Methyl-2(3H)-Furanone. a. Structure of interaction between Lipoxygenase and 5-Methyl-2(3H)-Furanone b. Interaction Lipoxygenase and 5-Methyl-2(3H)-Furanone 3D structure. c. Interaction Lipoxygenase and 5-Methyl-2(3H)-Furanone 2D structure

5-Methyl-2 (3H) -Furanone binds to lipoxygenase o the active sites of Gln329, Arg518, Ile330, Leu153, Glu146, Asn328, and Asp290. The three bioactive compounds tamarin bind to lipoxygenase with hydrogen, hydrophobic and van der Waals forces.

Table 1. Interaction Lipoxygenase and 5-Methyl-2(3H)-Furanone

Interaction	Energiy (Kcal/mol)	Name	Distance (A)	Type of Bond	Tipe of Bond	atom Donor	Atom Acceptor
Lipoxygenase - 5-Methyl-2(3H)-Furanone	-6	A:GLN329:HN - :LIG1:O	2,7226	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
		B:ARG518:HH21- :LIG1:O	2,6442	Hydrogen Bond	Conventional Hydrogen Bond	H-Donor	H-Acceptor
		:LIG1:C - A:ILE330	4,5131	Hydrophobic	Alkyl	Alkyl	Alkyl

Interaction 5-Methyl-2 (3H) –Furanone and lipoxygenase showed three main active site of the protein they are Gln329, Arg518 and Ile330. These interaction will bring positive impact to inhibit the protein. Based on in vivo study found that giving ethanol extract *Tamarindus indica* orally on mice provide analgesic effect on mice by thermal induction (Putri, 2017). It has hydrogen bonds and hydrophobic, bonds which make a strong binding and stabilize the protein-ligand binding, respectively (Bare, Kuki, et al., 2019; Bare, Sari, et al., 2019). The specificity in the -Methyl-2 (3H) –Furanone and lipoxygenase binding is the presence of hydrogen bond, which effect in improving ligand efficiency (Ferreira De Freitas & Schapira, 2017; Novoseletsky et al., 2010; Raharjo et al., 2014).

CONCLUSION

The results showed 5-Methyl-2 (3H) -Furanone binds to lipoxygenase on the active sites of LOX and produced energy -6Kcal/mol. The interactions that occur between compounds contained in *Tamarindus indica* have potential as inhibitors of LOX and are predicted to be used as compounds for inflammatory therapy.

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