

The Potential of Acetylfuran and Furfural from *Tamarindus indica* as Lipoxygenase Inhibitor: In Silico Study

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Abstract

Background: *Tamarindus indica* is a type of plant sub-family *Caesalpinioideae*, which is predicted to have anti-inflammatory properties. When inflammation occurs, arachidonic acid will undergo metabolism, the LOX pathway will release 5-lipoxygenase (5-LOX). **Objective:** This study aimed to analyze the potential of acetylfuran and furfural compounds on LOX action. **Methods:** The compound Acetylfuran (CID 14505), Furfural (CID 7362) were downloaded from the PubChem database. The 5-LOX protein was obtained from PDB (6N2W), preparation by removing ligands and molecules that bind to Discovery Studio V19.1.0.18287. Compound and protein interactions have interacted with the Vina autodock software integrated into the PyRX software and analyzed by Discovery Studio V19.1.0.18287. **Results:** The results showed that the content of Acetylfuran and Furfural compounds in *Tamarindus indica* is predicted to have the potential as an inhibitor of the LOX gene on different amino acid residues, namely 3 amino acid residues and 4 amino acid residues, respectively and produce binding energy. In addition, van der Waals forces, hydrogen and hydrophobic bonds were found, giving the strength of the bonds formed. **Conclusion:** Bioactive acetylfuran and furfural have the potential as a drug to curve inflammation in the human body.

Keywords: amino acid, anti-inflammatory, inflammation, lox, *Tamarindus indica*

Abstrak

Pendahuluan: *Tamarindus indica* merupakan jenis tumbuhan sub-famili *Caesalpinioideae* diprediksi memiliki sifat anti inflamasi. Saat terjadi inflamasi, asam arakidonat akan mengalami metabolisme, jalur LOX akan melepaskan 5-lipoxygenase (5-LOX). **Tujuan:** Penelitian ini bertujuan untuk menganalisis potensi senyawa asetilfuran dan furfural terhadap LOX. **Metode:** Senyawa Acetylfuran (CID 14505), Furfural (CID 7362) diunduh dari database PubChem. Protein 5-LOX diperoleh dari PDB (6N2W), preparasi dengan menghilangkan ligan dan molekul yang mengikat Discovery Studio V19.1.0.18287. Interaksi senyawa dan protein berinteraksi dengan perangkat lunak autodock Vina yang terintegrasi dalam perangkat lunak PyRX dan dianalisis oleh Discovery Studio V19.1.0.18287. **Hasil:** Hasil penelitian menunjukkan bahwa kandungan senyawa Acetylfuran dan Furfural yang terkandung dalam *Tamarindus indica* diperkirakan berpotensi sebagai penghambat gen LOX dengan melakukan pengahambatan pada residu asam amino yang berbeda, yaitu masing-masing 3 residu asam amino dan 4 residu asam amino dan menghasilkan ikatan energi. Selain itu, gaya van der Waals, ikatan hidrogen dan hidropobik ditemukan yang memberi kekuatan ikatan yang terbentuk. **Kesimpulan:** Bioaktif asetilfuran dan furfural berpotensi sebagai obat untuk mengatasi peradangan pada tubuh manusia.

Kata kunci: antiinflamasi, asam amino, inflamasi, lox, *Tamarindus indica*

INTRODUCTION

Tamarindus indica is a type of sub-family Caesalpinioideae plant belonging to the Fabaceae family (Adeola *et al.*, 2010; Bhadoriya *et al.*, 2011). The essential component obtained from *Tamarindus indica* L is part of the plant used in the pharmaceutical, food, chemical, and textile industries (Borquaye *et al.*, 2020). The people used tamarin as a pharmaceutical therapy because of the polyphenol content. The bioactive compounds are proanthocyanidin (apigenin, catechin, procyanidin B2, epicatechin, procyanidin dimer, procyanidin trimer), taxifolin, eriodictyol, and naringenin (Adeola *et al.*, 2010). Rossini's study in Putri (2017) discovered an analgesic effect in mice induced by *Tamarindus*' oral ethanol extract. Because *Tamarindus indica* is thought to have anti-inflammatory properties, this study provides information on reduced oedema in the legs of experimental animals. (Bhadoriya, 2012; Komakech *et al.*, 2019).

Inflammation is one sign in the human body because of the immune system from the infection or injury (Abdulkhaleq *et al.*, 2018). When inflammation occurs, there are differences in protein expression, where the amount of protein expressed is less when compared to healthy conditions (Bare *et al.*, 2018). The inflammatory response is the activation of signalling pathways that regulate levels of inflammatory mediators in tissue cells (Bare *et al.*, 2019; Chen *et al.*, 2018). During inflammation, there is a process of releasing arachidonic acid, which is an inflammatory mediator, which undergoes metabolism through different pathways, namely cyclooxygenase (COX) (Sari *et al.*, 2019) and the lipoxygenase (LOX) pathway. The LOX pathway will release 5-lipoxygenase (5-LOX), 12-lipoxygenase (12-LOX), and 15-lipoxygenase (15-LOX). The products of the COX pathway are prostaglandins (acute inflammatory mediators) and thromboxane, while those from the LOX pathway are leukotrienes and hydroperoxy fatty acids (Andriyono, 2019; Mueller *et al.*, 2010). In decreasing inflammation in the body, it is necessary to control genes that increase inflammation, one of which is LOX.

Recent studies have shown the potential for LOX as a target for inflammatory therapy (Al-u'datt u'datt *et al.*,

2019). Previous research has explained that the LOX group is used as a good anticancer target, but there has been no further study on this (Putri, 2017). Therefore, clinical trials in cancer patients are initiated with the LOXL2 monoclonal antibody, and several LOX/LOXL2 drug development programs are underway, approaching clinical trials in patients (Mayorca-Guiliani & Erler, 2013). Study of the role of *Tamarindus indica* in various chemical mediators, various cytokines and various chemical mediators that play a role in increasing the inflammatory process (Putri, 2017). This study aimed to analyze the potential of acetylfuran and furfural compounds on LOX action.

The introduction contains the background and objectives of the study. In addition, it can also include research reviews that have been done before by other researchers that are relevant to current research.

MATERIALS AND METHODS

Materials

The compounds Acetylfuran (CID 14505), Furfural (CID 7362) were downloaded from the PubChem database. The 5-LOX protein was downloaded from PDB (6N2W) and prepared by removing ligands and molecules that bind to Discovery Studio V19.1.0.18287.

Method

The compounds and proteins were interacted with the Vina autodock software integrated into the PyRX software and analyzed using Discovery Studio 9.1.0.18287 (Tiring *et al.*, 2019).

RESULTS AND DISCUSSION

Lipoxygenase (LOX) is an enzyme that oxidizes arachidonic acid to produce leukotriene (LTs), which indicates inflammation in cells. We found several amino acids that were formed between acetylfuran-lipoxygenase interactions. They are Gln549, Thr366, Thr371, Val553, Val243, Arg370, Ile365, Leu244, and Ser447 (Figure 1). The ligand and proteins are formed in the form of van der Waals forces (Gln549, Thr371, Val553, Ile365, Leu244, Ser447), Carbon Hydrogen Bond in the amino acid residue (Thr366) and *Pi-Alkyl* (Val243 and Arg370) with energy binding around -6,7Kcal/mol (Table 1).

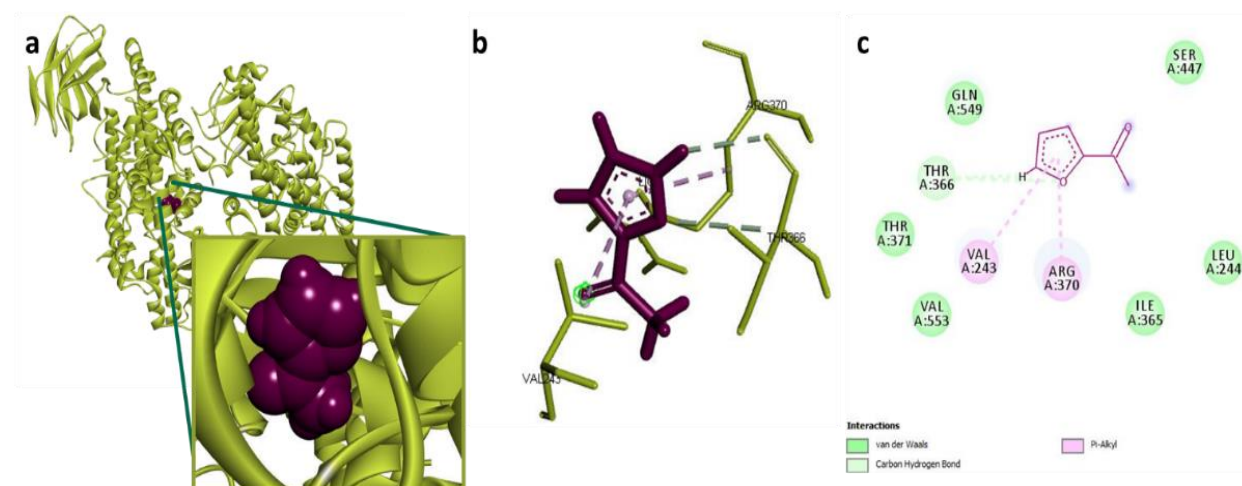


Figure 1. Interaction lipoxigenase-acetylfuran. a. structure of interaction between lipoxigenase-acetylfuran b. interaction lipoxigenase-acetylfuran 3D structure. c. interaction lipoxigenase-acetylfuran 2D structure

Table 1. Interaction between bioactive compounds of *Tamarindus indica* L and lipoxigenase

Interaction	Energy (Kcal/mol)	Name	Distance(A)	Type	Type Bond	atom Donor	Atom Acceptor
Lipoxygenase -Acetylfuran	-6,7	A:THR366: CA - :LIG1:O	3,768	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
		:LIG1:H - A:THR366: O	2,5265	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
		:LIG1 - A:VAL243	4,5012	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
		:LIG1 - A:ARG370	4,0319	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
Lipoxygenase -Furfural	-6,5	:LIG1:H - A:THR366: O	2,5535	Hydrogen Bond	Carbon Hydrogen Bond	H-Donor	H-Acceptor
		A:ARG370: NH2 - :LIG1	4,5703	Electrostatic	Pi-Cation	Positive	Pi-Orbitals
		A:VAL243: CG2 - :LIG1	3,6773	Hydrophobic	Pi-Sigma	C-H	Pi-Orbitals
		:LIG1 - A:ARG370	4,7349	Hydrophobic	Pi-Alkyl	Pi-Orbitals	Alkyl
		A:GLN549: HE21 - :LIG1:O	1,6623	Unfavorable	Unfavorable Bump; Conventional Hydrogen Bond	Steric; H-Donor	Steric; H-Acceptor

The interactions that occur between the compounds contained in *Tamarindus indica* have the potential as inhibitors of LOX. Research by Bare *et al.* (2019) reported the role of quinic acid on amino acid residues (Glu140, Asn144, Ser143, and Trp139) and B domain proteins (Glu236, Thr237, Lys333, Gln241, Gln330, Phe329, and Leu238) in the COX-2 gene. When compared with the studies in this study, it was found that there were very significant differences in the interacting amino acid residues. Each chemical component has a different interaction with the amino acid residue of LOX, which is found in Gln549, which is very specific

only in the Lipoxygenase-Furfural interaction. The two bioactive equations that bind Lipoxygenase to the amino acid residue of Thr366 is hydrogen bonds, Val243 are hydrophobic bonds, and Arg370 are Pi-Alkyl and Pi-Cation, respectively. The role of acetylfuran and furfural contained in *Tamarindus indica* is predicted at the molecular level. *Tamarindus indica* has a role in biomolecular vascular changes, endothelial receptor/endothelial cell contraction, the formation of endothelial gaps and the formation of bridges between cells (Putri, 2017).

Molecular tissue-level therapy against LOX family members can inhibit pro-tumoral activity by minimizing side effects and resistance (Mayorca-Guiliani & Erler, 2013). So that therapy for LOX is predicted to have a good success rate, thereby reducing the level of inflammation in the patient's body. The content of Acetylfuran and Furfural compounds in *Tamarindus indica* is predicted to have potential as an inhibitor of the LOX gene on different amino acid residues, namely three amino acid residues and four amino acid residues acid residues, respectively and producing binding energy. In addition, van der Waals forces, hydrogen and hydrophobic bonds were found, which gave the strength of the bonds formed.

CONCLUSION

In this study, we concluded that the acetylfuran and furfural compounds have a positive impact as inhibitor LOX. The interaction inhibits LOX and has an essential role in curving the inflammatory disease.

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