

# Potential Molecular Interaction of Nutmeg's *Myristica fragrans* Active Compound via Activation of Caspase-3

*by Ronny Lesmana*

---

**Submission date:** 22-Jun-2022 01:06PM (UTC+0800)

**Submission ID:** 1861135588

**File name:** yristica\_fragrans\_Active\_Compound\_via\_Activation\_of\_Caspase-.pdf (628.1K)

**Word count:** 4247

**Character count:** 23956



## Potential Molecular Interaction of Nutmeg's (*Myristica fragrans*) Active Compound via Activation of Caspase-3

Ronny Lesmana<sup>1,2,\*</sup>, Filza Yulina Ade<sup>1</sup>, Yuni Susanti Pratiwi<sup>1,2</sup>, Hanna Goeanawan<sup>1,2</sup>, Nova Sylviana<sup>1,2</sup>, Sandra Megantara<sup>3</sup>, Susianti Susianti<sup>1</sup>, Vita Murniati Tarawan<sup>1,2</sup>, Purwo Sri Rejeki<sup>4</sup>, Hamidie Ronald Daniel Ray<sup>5,6</sup>, Unang Supratman<sup>7</sup>

<sup>1</sup>Biological Activity Division, Central Laboratory, Universitas Padjadjaran, Indonesia

<sup>2</sup>Physiology Division, Department of Biomedical Sciences, Faculty of Medicine, Universitas Padjadjaran, Indonesia

<sup>3</sup>Department of Pharmaceutical Analysis and Medicinal Chemistry, Faculty of Pharmacy, Universitas Padjadjaran, Indonesia

<sup>4</sup>Physiology Division, Department of Medical Physiology and Biochemistry, Faculty of Medicine, Universitas Airlangga, Indonesia

<sup>5</sup>Departement of Sport Science, Faculty of Sport and Health, Universitas Pendidikan Indonesia, Indonesia

<sup>6</sup>Kanazawa University, Ishikawa, Japan

<sup>7</sup>Department of Chemistry, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Indonesia

\*Correspondence: E-mail: [ronny@unpad.ac.id](mailto:ronny@unpad.ac.id)

### ABSTRACTS

*Myristica fragrans* Houtt (belongs to the Myristicaceae family) is a Maluku Island (Indonesia) native plant. The seed of *M. fragrans* (Nutmeg) has been used for medicinal benefits. *M. fragrans* also has anti-cancer properties. The goal of this research was to use computer-aided drug design to investigate the in silico molecular docking of selected nutmeg compounds against Caspase-3. Molecular docking using Malegro Virtual Docker (MVD) software Ver 5.5 was performed to investigate binding complicated models to offer information on critical drug-receptor interactions. The most potent ligand was Licarin B, which had a docking score of -103.07 kcal/mol. The Licarin B structure formed several hydrogen bonds with Trp214 and Phe250. These findings imply that the nutmeg seed contains a prospective compound that could be a great anti-cancer agent.

© 2022 Tim Pengembang Jurnal UPI

### ARTICLE INFO

#### Article History:

Received 10 Mar 2022

Revised 19 Apr 2022

Accepted 26 Apr 2022

Available online 27 Apr 2022

#### Keyword:

Anticancer,  
Caspase-3,  
Molecular docking,  
*Myristica fragrans*.

## 1. INTRODUCTION

<sup>15</sup> *Myristica fragrans* Houtt. (Myristicaceae) is an evergreen tree that produces nutmeg and mace (Kusuma et al., 2020; Ha et al., 2020). The aromatic evergreen tree (*M. fragrans*) has long been utilized as a spice in the culinary world (Ha et al., 2020). Nutmeg (the seed of *M. fragrans*), a Maluku Island (Indonesia) native plant, has been utilized in traditional medicine for a long time (Susianti et al., 2021).

*M. fragrans* has long piqued the interest of pharmacologists and chemists due to its widespread culinary and folk medicinal applications. Several investigations have found that *M. fragrans* contains a wide range of phytochemicals, including lignans, neolignans, terpenoids, diphenylalkanes, flavonoids, and phenylpropanoids, all of which have pharmacological effects (Fatimah et al., 2019; Ha et al., 2020; Ebulue, 2022).

*M. fragrans* exhibits many biological properties, including anticancer (Abourashed & El-Alfy, 2016; Le et al., 2017), antioxidants, antibacterial (Matulyte et al., 2020), analgesics (Mishra et al., 2018), and antidiabetic (Lestari et al., 2019). Extracts and a variety of chemicals from the nutmeg seed have been found to have anti-cancer and antioxidant properties in several studies (Zhang et al., 2015; Abbas & Baig, 2020).

Cancer is one of the most common health related search topics in the world (Yousaf et al., 2021). Skin cancer prevention property is caused by a flavonoid present in nutmeg that has anti-cancer properties (Chen et al., 2012). Skin cancer (melanoma) has been on the rise in recent years as a result of UV exposure (Ika & Hery, 2021).

Skin cancer induced by excessive UV radiation from the sun is almost as severe as skin cancer caused by others (Chavda & Bhatt, 2019). Environmental factors cause melanoma cancer to grow more quickly than non-melanoma cancer (Ika & Hery, 2021). Melanoma is a skin cancer that develops

from the aberrant multiplication of melanocyte cells, which generate melanin. This cancer has a high level of aggressiveness and is potentially fatal (Linares et al., 2015; Davis et al., 2019). Melanoma skin cancer has a high proclivity for spreading to other regions of the body, making treatment challenging (Ika & Hery, 2021). The development of novel bioactive chemicals is highly important (Ebulue, 2023). Specifically, chemicals with highly specific anti-cancer action are critical important in the treatment of cancer (Ika & Hery, 2021). Myristicin's anti-cancer properties were anticipated using computer-assisted molecular docking.

Molecular docking is a problem-solving or simulation approach used to aid in the early phases of drug development (Altaf et al., 2022; Maripul, 2017). In structural molecular biology and computer-assisted drug creation, molecular docking is an important technique (Morris et al., 2008). Molecular docking is a technique for determining the activity and affinity of small compounds by anticipating their binding orientation to their protein targets (Ika & Hery, 2021).

Several anti-cancer molecular docking studies using phytochemical ingredients have previously been published (Kirishnamaline et al., 2021; Ibrahim & El-Banna, 2021; Galal et al., 2011). Caspase-3 is a key player in apoptosis, cleaving a variety of protein substrates in cells and causing cell death when activated. Because several chemotherapeutics have been shown to induce apoptosis in cancer cells, promoting or activating apoptosis by targeting apoptosis regulators has been recommended as a possible technique for anticancer drug development. *M. fragrans'* anti-cancer activity via caspase-3 has not been molecularly docked before.

<sup>6</sup> Based on our previous studies (Ray et al., 2021a; Ray et al., 2021b; Masuda et al., 2017), here in this study, we have conducted the molecular interaction selected *M. fragrans* seed constituents as anticancer

agents against caspase-3. A docking score was also evaluated for investigating the anti-cancer activity.

## 2. METHODS

The structure of caspase 3 (was obtained from the Protein Data Bank (PDB ID: 4DCP; [www.rcsb.org/structure/4DCP](http://www.rcsb.org/structure/4DCP)) (Kang *et al.*, 2012) and the isolated constituents from *Myristica fragrans* Seeds (Matulyte *et al.*, 2019) were prepared using ChemDraw ver 16.0.1.4 (61) (Cambridge Soft). The receptor-ligand interactions were identified and calculated using molecular docking.

AutoGrid was used to create the grid map, which included a grid box and a docking box. A genetic algorithm with local search was used to calculate the docking possibilities. The ligands were docked using Molegro Virtual Docker (MVD) Ver 5.5 utilizing a blind docking method to include the full potential binding site.

The binding free energy (kcal/mol) was used to calculate the binding affinity. The value of free binding energy can be determined by using Notepad++ to examine the docking "dock.dlg" file. The lowest bond energy affinity for each docking result was found by looking at the histogram for each cluster—the lower the energy, the stronger the relationship. AutoDockTools was used to visualize the conformation of molecular docking data.

The PyMOL Visualization Tool and the Molegro 5.5 program are used to visualize the bonds that occur between the ligands of each macromolecule. The ideal post-docking compound structure must have the lowest energy and the molecules must be at the same active site as the native ligand, as visible in the protein structure. For the pose with the highest score, observations of ligand-protein interactions were made, including hydrogen bond interactions, steric (van der Waals) interactions, and electrostatic interactions.

## 3. RESULTS AND DISCUSSION

The interaction between two molecules is anticipated using molecular docking, a technique utilized in drug discovery and medicinal chemistry. In drug development, docking is the process of connecting a small molecule (ligand) with protein (enzyme). The binding energy is calculated using molecular mechanics in most docking programs (Prieto-martinez *et al.*, 2018). Virtual screening, pose prediction, calculation-ligand and binding conformation affinity are all phases in molecular docking (Guedes *et al.*, 2013). Molecular docking is useful in drug design since it allows users to find the best conformation and orientation of the ligand-protein complex (Ika & Hery, 2021). The ligand must have the lowest free energy score to be effective in selecting therapeutic candidates (Gaba *et al.*, 2015).

Molecular docking provides many advantages, including the ability to evaluate large compound databases at a lower cost than experiments (Vlasiou & Pafiti, 2021). The optimal structure is utilized to forecast the constituent probable mode and find the direction of the ideal pose using molecular modeling (Lin *et al.*, 2020). Root mean square deviation (RMSD) and visual position are used to evaluate validation parameters. The reliability and reproducibility of the new docking technique were first verified by redocking ligands at the active receptor site using the RMSD measurement.

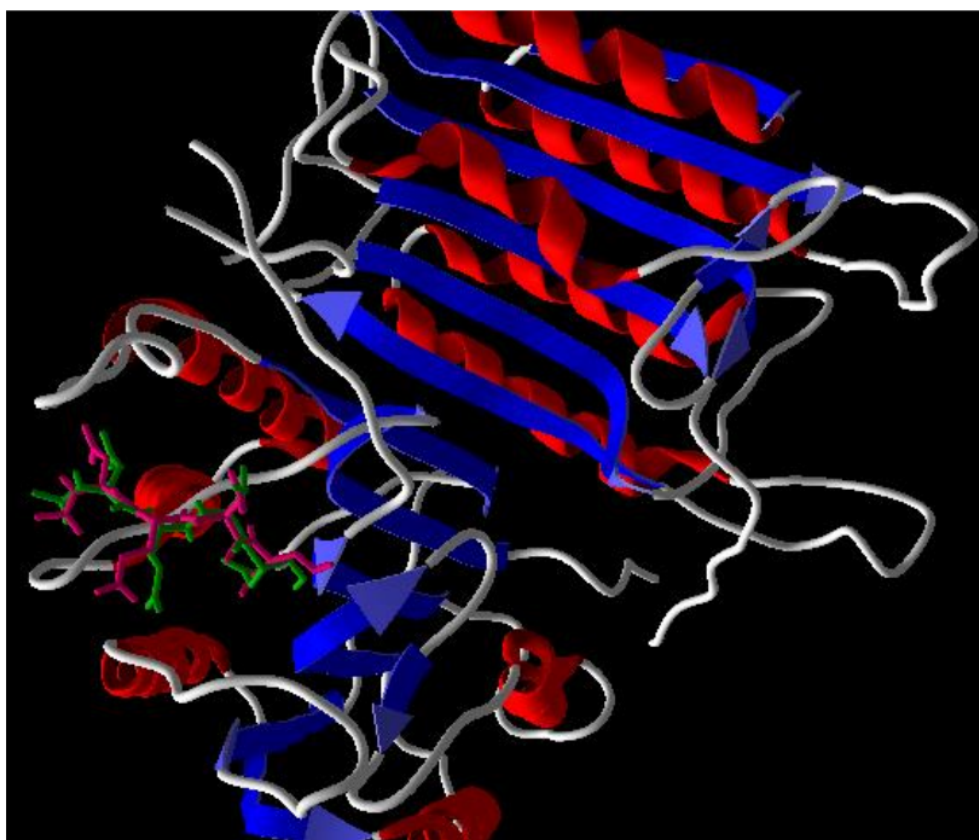
The RMSD is a measure of precision with reliable findings for repeated assays. It is the difference between the expected and observed experimental values. When compared to the crystallographic structure, an RMSD value less than 2.0 indicates that the algorithm is viable (Osman *et al.*, 2020). This research might continue utilizing our verified docking approach (Sargolzaei, 2021), as can be shown from the comparison of our RMSD with the RMSD indicated above. The creation of the best-quality docking



mechanism is indicated by an RMSD of less than 2.0 (Ghosh *et al.*, 2021).

A molecular docking study was performed using Malegro Virtual Docker (MVD) software version 5.5. Criteria of acceptance are set with the value of RMSD less than 2.0 Å (Figure 1) The docking program is used to look into the inhibitor's potential binding mechanism to the nutmeg constituents. Nutmeg seed essential oil contains anticarcinogenic effects. The nutmeg seed oil has a wide range of compositions depending on where it's sourced (Ika & Hery, 2021, Nikolic *et al.*, 2021).

Ten compounds of nutmeg seed were docked to the binding site with the stimulant caspase-3. Caspase-3 activation as an apoptosis effector is one of the apoptosis signaling pathways (Li & Yuan, 2008). Apoptosis is a type of cell death that can be induced by both endogenous and external triggers (Sharifi-Rad *et al.*, 2017). Extrinsic and intrinsic apoptosis are the two basic types of apoptosis signaling mechanisms. Intrinsic apoptosis pathways are activated by most anticancer actions (Lu *et al.*, 2017; Wicaksono *et al.*, 2015; Rizal & Sandra, 2016).



**Figure 1.** The binding orientation between the native ligand (green) and the docking result simulation (purple) by MVD. The RMSD is 1.24Å.

The Pass online and molecular docking results were presented in **Table 1**. It indicates that the compounds from nutmeg are Piperitol, Myristicin, Licarin B, Isoelemicin, and Methylisoeugenol showed the best anti-cancer activity with a Probably active (Pa) value above 0.7, the compounds were believed to play a role in preventing the proliferation of cancer cells via the stimulant caspase-3 pathway. With pass online software, the findings in silico are also linear; five compounds have a rank score of less than 0.7.

The compound expected to actively block Caspase 3 production enzymes has a score ranging from -65.70 to -103.07 kcal/mol. As shown in **Table 1**, all nutmeg seed compounds performed significantly better as active substances of nutmeg. The anti-cancer activity correlates to the predicted binding energy (Rahman *et al.*, 2021)

The docking score between caspase-3 and compound of Methylisoeugenol, Isoelemicin, Myristicin, Piperitol, and Licarin B was -65.79, -69.10, -74.80, -91.71, -103.07, respectively. The docking score is a prediction of the inhibitory activity based on the binding affinity between receptor and ligand as determined by the optimal algorithm. The docking score's major importance is the evaluation index for quick preliminary steps and inhibitors (Ika & Hery, 2021). The docking score for the protein-ligand complex is used to estimate the free binding free energy. The highest protein affinity with the strongest powerful ligand equals the best docking scores (Rahman *et al.*, 2021).

**Table 1** shows the interaction of nutmeg compound and stimulant caspase-3. **Table 1**

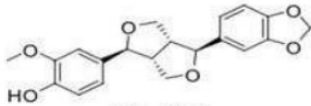
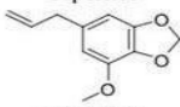
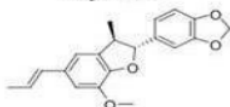
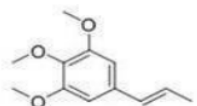
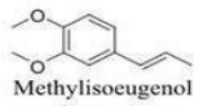
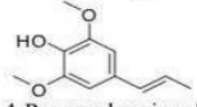
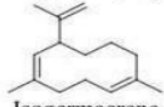
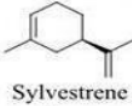
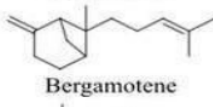
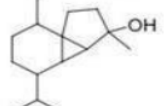
shows the interacting hydrogen bond and steric interaction (non-hydrogen bond) from the nutmeg compound. Docking simulation colored 2D-binding mode representation between caspase-3 and compound of nutmeg shown in **Figure 2**. The binding interaction between the bioactive compound of nutmeg and stimulant caspase-3 was verified by molecular docking.

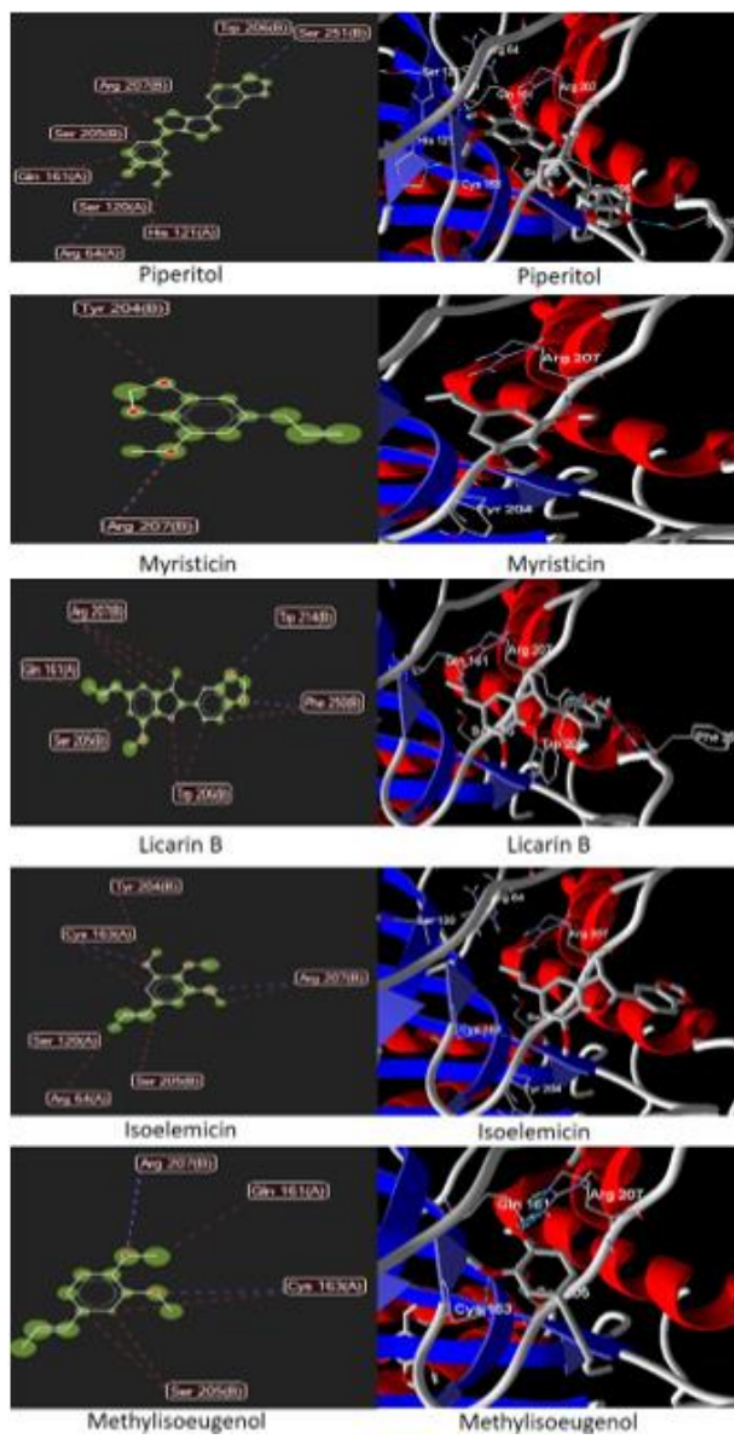
**Figure 2** shows the two-dimensional interaction of the bioactive compound of nutmeg and stimulant caspase-3. There is no hydrogen bond interaction formed in Isogermacrene, Sylvestrene, Bergamotene, and Cubebol. This component has a low Pa score of less than 0.6.

This is thought to be a molecule that plays a little function in cancer cell proliferation prevention. On other hand, five others (Piperitol, Myristicin, Licarin B, Isoelemicin, and Methylisoeugenol) have great potency as inhibitor caspase-3 according to the higher Pa value. Specifically, Licarin B has the greatest Pa value of all the active nutmeg compounds, and it has hydrogen bonds with Trp214 and Phe250.

The nutmeg components and inhibitor binding mechanism were clearly understood and visualized as a result of the molecular docking studies (Ika & Hery, 2021). Inhibition may be mediated by the same binding location and manner (Zou *et al.*, 2018). The most extensively used approach for structure-based drug design is molecular docking, which offers a wide range of applications, including binding energies and interactions (Zhang *et al.*, 2017).

**Table 1.** Pass online and molecular docking result.

Compound	Pa (Caspase-3 stimulant)	Re-rank Score (kcal/mol)	Hydrogen Bond Interaction	Steric Interaction
 Piperitol	0,923	-91,71	Arg 64; Ser 120; Arg 207; Ser 251	His 121; Gln 161; Ser 205; Arg 207; Trp 251
 Myristicin	0,911	-74,80	Arg 207	Tyr 204
 Licarin B	0,897	-103,07	Trp 214; Phe 250	Gly 161; Ser 205; Trp 206; Arg 207;
 Isoelemicin	0,751	-69,10	Cys 163; Arg 207	Arg 64; Ser 120; Cys 163; Tyr 204; Ser 205; Arg 207
 Methylisoeugenol	0,732	-65,79	Cys 163; Arg 207	Gln 161; Cys 163; Ser 205
 4-Propenyl syringol	0,688	-58,71	His 121; Cys 163; Arg 207	Gln 161; Cys 163; Ser 205; Trp 206
 Isogermacrene	0,545	-55,55	-	Ser 205 Arg 207
 Sylvestrene	0,537	-52,14	-	Gln 161 Ser 205 Arg 207
 Bergamotene	0,361	-31,37	-	Gln 161; Ser 205; Arg 207
 Cubebol	0,272	-20,19	-	His 121; Gln 161; Cys 163; Ser 205; Arg 207



**Figure 2.** The binding interaction between the bioactive compound of nutmeg and stimulant caspase-3.



#### 4. CONCLUSION

Molecular docking of selected compounds from nutmeg (*M. fragrans*) exhibit that five constituents have great potency as an inhibitor of caspase-3. The best interaction model of the nutmeg compound was shown by Licarin B with a binding energy score of -103.07 kcal/mol. Licarin B has the greatest Pa value of all the active nutmeg compounds, and it has hydrogen bonds with Trp214 and Phe250. These findings implicated that

nutmeg contains great compounds which could actively block the caspase-3 activity, and could be further developed as a potent compound against cancer (potential as anti-cancer).

#### 5. AUTHORS' NOTE

The author(s) declare(s) that there is no conflict of interest regarding the publication of this article. The authors confirmed that the data and the paper are free of plagiarism.

#### 6. REFERENCES

- Abbas, S. R., and Baig S. (2020). Treatment of skin cancer by medicinal plants [A review]. *Journal of Biotechnological Sciences*, 137(2),131–137.
- Abourashed, E. A., and El-Alfy, A. T. (2016). Chemical diversity and pharmacological significance of the secondary metabolites of nutmeg (*Myristica fragrans* Houtt.). *Phytochemistry Reviews: Proceedings of the Phytochemical Society of Europe*, 15(6), 1035–1056.
- Altaf, R., Ullah, Z., Darko, D. A., Iqbal, A., Khan, M. S., and Asif, M. (2022). Molecularly imprinted polymers for the detection of chlorpyrifos (an organophosphate pesticide). *ASEAN Journal of Science and Engineering*, 2(3), 257-266.
- Chavda, J., and Bhatt, H. (2019). 3D-QSAR (CoMFA , CoMSIA , HQSAR and topomer CoMFA), MD simulations and molecular docking studies on purinylpyridine derivatives as B- Raf inhibitors for the treatment of melanoma cancer. *Structural Chemistry*, 30, 2093-2107.
- Chen, H., Yao, K., Nadas, J., Bode, A. M., Malakhova, M., Oi, N., Li, H., Lubet, R. A., and Dong, Z. (2012). Prediction of molecular targets of cancer preventing flavonoid compounds using computational methods. *PLoS One*, 7(5), 1-9.
- Davis, E. J., Perez, M. C., Ayoubi, N., Zhao, S., Ye, F., Wang, D. Y., Sosman, J. A., Al-Rohil, R. N., Eroglu, Z., and Johnson, D. B. (2019). Clinical correlates of response to anti-PD-1-based therapy in patients with metastatic melanoma. *Journal of Immunotherapy*, 42(6), 221-227.
- Ebulue, M. M. (2022). Bioactive compounds and antioxidant activity of ethanol leaf extract of Eucalyptus Tereticornis. *ASEAN Journal Science and Engineering*, 3(1), 69-78.
- Ebulue, M. M. (2023). Bioactive compounds and antioxidant activity of ethanol leaf extract of eucalyptus tereticornis. *ASEAN Journal of Science and Engineering*, 3(1), 69-78.

- Fatimah, S., Hasimah A., and Norhayati, D. (2019). Phytochemical screening of *Sargassum sp* and in vitro seed germination test. *Indonesian Journal Science and Technology*, 4(1), 48-54.
- Gaba, M., Shaheed, A., Ajit, B., Jujhar, S., and Memorial, S. (2015). An overview on molecular docking international journal of drug development and research. *JSM Chem*, 4(2), 1024-1028.
- Galal, S. A., Abdelsamie, A. S., Tokuda, H., Suzuki, N., Lida, A., Elhefnawi, M. M., Ramadan, R. A., Atta, M. H., and El Diwani, H. I. (2011). Part I: Synthesis, cancer chemopreventive activity and molecular docking study of novel quinoxaline derivatives. *European Journal of Medicinal Chemistry*, 46(1), 327-340.
- Ghosh, P., Bhakta, S., Bhattacharya, M., Sharma, A. R., Sharma, G., Lee, S. S., and Chakraborty, C. (2021). A novel multi-epitopic peptide vaccine candidate against *Helicobacter pylori*: in-silico identification, design, cloning and validation through molecular dynamics. *International Journal of Peptide Research and Therapeutics*, 27(2), 1149-1166.
- Guedes, I. A., de Magalhães, C. S., and Dardenne, L. E. (2014). Receptor-ligand molecular docking. *Biophysical Reviews*, 6(1), 75-87.
- Ha, M. T., Vu, N. K., Tran, T. H., Kim, J. A., Woo, M. H., and Min, B. S. (2020). Phytochemical and pharmacological properties of *Myristica fragrans* Houtt.: an updated review. *Archives of Pharmacal Research*, 43(11), 1067-1092.
- Ibrahim, R. S., and El-Banna, A. A. (2021). Network pharmacology-based analysis for unraveling potential cancer-related molecular targets of Egyptian propolis phytoconstituents accompanied with molecular docking and in vitro studies. *RSC Adv*, 11(19), 11610-11626.
- Ika, N. F., and Hery, M. A. (2021). Molecular docking study of nutmeg (*Myristica fragrans*) constituents as anti-skin cancer agents. *Jurnal Kimia dan Pendidikan Kimia*, 6(1), 14-22.
- Kang, H. J., Lee, Y. M., Jeong, M. S., Kim, M., Bae, K. H., Kim, S. J., and Chung, S. J. (2012). Molecular insight into the role of the leucine residue on the L2 loop in the catalytic activity of caspases 3 and 7. *Bioscience Reports*, 32(3), 305-313.
- Kirishnamaline, G., Magdaline, J., D., Chithambarathanu, T., Aruldas, D., and Anuf, A., R. (2021). Theoretical investigation of structure, anti-cancer activity and molecular docking of thiourea derivatives. *Journal of Molecular Structure*, 1225, 1-24.
- Kusuma, J., Scarcelli, N., Couderc, M., Mariac, C., Zekraoui, L., and Duminil, J. (2020). Microsatellite markers development for Indonesian nutmeg (*Myristica fragrans* Houtt.) and transferability to other Myristicaceae spp. *Molecular Biology Reports*, 47(6), 4835-4840.
- Le, T. V. T., Nguyen, P. H., Choi, H. S., Yang, J. L., Kang, K. W., and Ahn, S. G. (2017). Diarylbutane-type lignans from *Myristica fragrans* (Nutmeg) show the cytotoxicity

against breast cancer cells through activation of AMP-activated protein kinase. *Natural Product Sciences*, 23(1), 21-28.

Lestari, K., Diantini, A., Barliana, M. I., Achmad, T. H., Subarnas, A., Mutaki, Abdulah, R., Lesmana, R., and Hwang, J. K. (2019). Potential natural dual agonist PPAR $\alpha$ / $\gamma$ -induced antidiabetic and antidyslipidemic properties of safrole-free nutmeg seed (*Myristica fragrans* Houtt) extract. *The Natural Product Journal*, 9, 248-253.

Li, J., and Yuan, J. (2008). Caspases in apoptosis and beyond. *Oncogene*, 27(48), 6194–6206.

Lin, X., Li, X., and Lin, X. (2020). A Review on Applications of Computational Methods in Drug Screening and Design. *Molecules (Basel, Switzerland)*, 25(6), 1-17.

Linares, M. A., Zakaria, A., and Nizran, P. (2015). Skin cancer. *Primary Care*, 42(4), 645–659.

Lu, X., Yang, L., Chen, J., Zhou, J., Tang, X., Zhu, Y., Qiu, H., and Shen, J. (2016). The action and mechanism of myrislignan on A549 cells in vitro and in vivo. *Journal of Natural Medicines*, 71, 76-85.

Marimpul, R. (2017). Effect of substrate temperature on quality of copper film catalyst substrate: A Molecular Dynamics Study. *Indonesian Journal of Science and Technology*, 2(2), 183-190.

Masuda, K., Jue, T., and Hamidie, R. D. R. (2017). Mitochondrial biogenesis induced by exercise and nutrients: Implication for performance and health benefits. *Indonesian Journal of Science and Technology*, 2(2), 221-229.

Matulyte, I., Jekabsone, A., Jankauskaite, L., Zavistanaviciute, P., Sakiene, V., Bartkiene, E., Ruzauskas, M., Kopustinskiene, D. M., Santini, A., and Bernatoniene, J. (2020). The essential oil and hydrolats from *Myristica fragrans* seeds with magnesium aluminometasilicate as excipient: Antioxidant, antibacterial, and anti-inflammatory activity. *Foods*, 9(1), 1-12.

Matulyte, I., Marksa, M., Ivanauskas, L., Kalvėnienė, Z., Lazauskas, R., and Bernatoniene, J. (2019). GC-MS analysis of the composition of the extracts and essential oil from *Myristica fragrans* seeds using magnesium aluminometasilicate as excipient. *Molecules*, 24(6), 1-12.

Mishra, A., Rahman, S. Z., and Khan, R. A. (2018). CNS Activity of *Myristica fragrans* Houtt. - An Experimental Study. *Bangladesh Journal of Medical Science*, 17(1), 98–106.

Morris, G. M., and Lim-Wilby, M. (2008). Molecular docking. *Methods in Molecular Biology*, 443, 365–382.

Nikolic, V., Nikolic, L., Dinic, A., Gajic, I., Urosevic, M., Stanojevic, L., and Danilovic, B. (2021). Chemical composition, antioxidant and antimicrobial activity of nutmeg (*Myristica fragrans* Houtt.) seed essential oil. *Journal of Essential Oil-Bearing Plants*, 24(2), 218-227.

- Osman, S. M., Ayoub, N. A., Hafez, S. A., Ibrahim, H. A., El Raey, M. A., El-Emam, S. Z., Seada, A. A., and Saaddeeen, A. M. (2020). Aldose reductase inhibitor from *Cassia glauca*: A comparative study of cytotoxic activity with Ag nanoparticles (NPs) and molecular docking evaluation. *PLoS One*, *15*(10), 1-24.
- Prieto-Martinez, F. D., Arciniaga, M., and Medina-Franco, J. L. (2018). Molecular docking: current advances and challenges. *TIP. Revista Especializada En Ciencias Químico-Biológicas*, *21*(1), 65-87.
- Rahman, F., Tabrez, S., Ali, R., Alqahtani, A. S., Ahmed, M. Z., and Rub, A. (2021). Molecular docking analysis of rutin reveals possible inhibition of SARS-CoV-2 vital proteins. *Journal of Traditional and Complementary Medicine*, *11*(2), 173–179.
- Ray, H. R. D., Nandiyanto, A.B.D., Patriasih, R., and Firmansah, A. (2021b). Nanocurcumin potential to increase mitochondrial biogenesis in skeletal muscle via AMPK-PGC-1alpha. *Journal of Engineering Research*, *9*(special issue), 1-15.
- Ray, H. R. D., Patriasih, R., and Sulastri, A. (2021a). Potential of nanocurcumin on cytokine storm through decreased IL-6 and TNF- $\alpha$  expression. *Malaysian Journal of Medicine and Health Sciences*, 115-119.
- Rizal, M. I., and Sandra, F. (2016). *Brucea javanica* leaf extract activates caspase-9 and caspase-3 of mitochondrial apoptotic pathway in human oral squamous cell carcinoma. *Indonesian Biomedical Journal*, *8*, 43-48.
- Sargolzaei M. (2021). Effect of nelfinavir stereoisomers on coronavirus main protease: Molecular docking, molecular dynamics simulation and MM/GBSA study. *Journal of Molecular Graphics and Modelling*, *103*, 1-18.
- Sharifi-Rad, J., Sureda, A., Tenore, G. C., Daglia, M., Sharifi-Rad, M., Valussi, M., Tundis, R., Sharifi-Rad, M., Loizzo, M. R., Ademiluyi, A. O., Sharifi-Rad, R., Ayatollahi, S. A., and Iriti, M. (2017). Biological Activities of Essential Oils: From Plant Chemoecology to Traditional Healing Systems. *Molecules*, *22*(1), 1-55.
- Susianti, S., Lesmana, R., Salam, S., Julaeha, E., Pratiwi, Y. S., Sylviana, N., Goenawan, H., Kurniawan, A., and Supratman, U. (2021) the effect of nutmeg seed (*M. Fragrans*) extracts induces apoptosis in melanoma maligna cell's (B16-F10). *Indonesian Biomedical Journal*, *13*(1), 68-74
- Vlasiou, M. C., and Pafiti, K. S. (2021). Screening possible drug molecules for Covid-19. The example of vanadium (III/IV/V) complex molecules with computational chemistry and molecular docking. *Computational Toxicology*, *18*, 1-8.
- Wicaksono, B. D., Tangkearung, E., and Sandra, F. (2015). *Brucea javanica* leaf extract induced apoptosis in human oral squamous cell carcinoma (HSC2) cells by attenuation of mitochondrial membrane permeability. *Indonesian Biomedical Journal*, *7*, 107-110.
- Yousaf, A., Tasneem, N., Mustafa, A., Fatima, R., Nabia, N., Khan, R.A., Abdulbasit, H., Abubakar, M., Asadullah, A., Rizwan, R. and Baqa-ur-Rehman, B. (2021). Gastric cancer



associated risk factors and prevalence in Pakistan. *ASEAN Journal of Science and Engineering*, 1(2), 73-78.

Zhang, C. R., Jayashree, E., Kumar, P. S., and Nair, M. G. (2015). Antioxidant and Anti-inflammatory Compounds in Nutmeg (*Myristica Fragrans*) Pericarp as Determined by in vitro Assays. *Natural Product Communications*, 10(8), 1299-1402.

Zhang, Y., Mao, X., Su, J., Geng, Y., Guo, R., Tang, S., Li, J., Xiao, X., Xu, H., and Yang, H. (2017). A network pharmacology-based strategy deciphers the underlying molecular mechanisms of Qixuehe Capsule in the treatment of menstrual disorders. *Chinese Medicine*, 12, 1-11.

Zuo, A. R., Dong, H. H., Yu, Y. Y., Shu, Q. L., Zheng, L. X., Yu, X. Y., and Cao, S. W. (2018). The antityrosinase and antioxidant activities of flavonoids dominated by the number and location of phenolic hydroxyl groups. *Chinese Medicine*, 13, 1-12.

# Potential Molecular Interaction of Nutmeg's Myristica fragrans Active Compound via Activation of Caspase-3

## ORIGINALITY REPORT

19%

SIMILARITY INDEX

15%

INTERNET SOURCES

12%

PUBLICATIONS

1%

STUDENT PAPERS

## PRIMARY SOURCES

1	<a href="http://mafiadoc.com">mafiadoc.com</a> Internet Source	4%
2	<a href="http://ejournal.upi.edu">ejournal.upi.edu</a> Internet Source	1%
3	<a href="http://www.japsonline.com">www.japsonline.com</a> Internet Source	1%
4	<a href="http://inabj.org">inabj.org</a> Internet Source	1%
5	<a href="http://vm36.upi.edu">vm36.upi.edu</a> Internet Source	1%
6	<a href="http://www.frontiersin.org">www.frontiersin.org</a> Internet Source	1%
7	<a href="http://riit.com.mx">riit.com.mx</a> Internet Source	1%
8	Submitted to Universitas Airlangga Student Paper	1%
9	<a href="http://pubs.rsc.org">pubs.rsc.org</a> Internet Source	1%

10	<a href="https://link.springer.com">link.springer.com</a> Internet Source	1 %
11	<a href="https://e-journal.unair.ac.id">e-journal.unair.ac.id</a> Internet Source	<1 %
12	Kaliyaperumal Ashokkumar, Jesus Simal - Gandara, Muthusamy Murugan, Mannananil Krishnankutty Dhanya, Arjun Pandian. " Nutmeg ( Houtt.) essential oil: A review on its composition, biological, and pharmacological activities ", <i>Phytotherapy Research</i> , 2022 Publication	<1 %
13	Mohsen Sargolzaei. "Effect of nelfinavir stereoisomers on coronavirus main protease: Molecular docking, molecular dynamics simulation and MM/GBSA study", <i>Journal of Molecular Graphics and Modelling</i> , 2021 Publication	<1 %
14	Unang Supratman, Supriatno Salam, Wiro Naibaho, Mohamad Fajar et al. "New cytotoxic limonoids from the stem bark of <i>Chisocheton pentandrus</i> (Blanco) Merr", <i>Phytochemistry Letters</i> , 2020 Publication	<1 %
15	Chuan-Rui Zhang, Ettannil Jayashree, Paramasivam Suresh Kumar, Muraleedharan G. Nair. " Antioxidant and Anti-inflammatory Compounds in Nutmeg ( ) Pericarp as	<1 %

## Determined by Assays ", Natural Product Communications, 2015

Publication

---

16

"Anticancer Plants: Natural Products and Biotechnological Implements", Springer Science and Business Media LLC, 2018

Publication

---

<1 %

17

"Bioactive Molecules in Food", Springer Science and Business Media LLC, 2019

Publication

---

<1 %

18

"Plant-derived Bioactives", Springer Science and Business Media LLC, 2020

Publication

---

<1 %

19

Raksha A. Kankariya, Ambalal B. Chaudhari, Navin D. Dandi. "Inhibitory efficacy of 2, 4-diacetylphloroglucinol against SARS-COV-2 proteins: in silico study", Biologia, 2022

Publication

---

<1 %

20

Said Tighadouini, Smaail Radi, Farid Abrigach, Redouane Benabbes, Driss Eddike, Monique Tillard. "Novel  $\beta$ -keto-enol Pyrazolic Compounds as Potent Antifungal Agents. Design, Synthesis, Crystal Structure, DFT, Homology Modeling, and Docking Studies", Journal of Chemical Information and Modeling, 2019

Publication

---

<1 %



21

Internet Source

&lt;1 %

22

[dspace.mist.ac.bd:8080](https://dspace.mist.ac.bd:8080)

Internet Source

&lt;1 %

23

[journals.ut.ac.ir](https://journals.ut.ac.ir)

Internet Source

&lt;1 %

24

[pubag.nal.usda.gov](https://pubag.nal.usda.gov)

Internet Source

&lt;1 %

25

[www.mdpi.com](https://www.mdpi.com)

Internet Source

&lt;1 %

26

[www.thieme-connect.com](https://www.thieme-connect.com)

Internet Source

&lt;1 %

27

Ai-Ren Zuo, Huan-Huan Dong, Yan-Ying Yu, Qing-Long Shu, Li-Xiang Zheng, Xiong-Ying Yu, Shu-Wen Cao. "The antityrosinase and antioxidant activities of flavonoids dominated by the number and location of phenolic hydroxyl groups", Chinese Medicine, 2018

Publication

&lt;1 %

28

Marcin Poreba, Aleksandra Szalek, Paulina Kasperkiewicz, Wioletta Rut, Guy S. Salvesen, Marcin Drag. "Small Molecule Active Site Directed Tools for Studying Human Caspases", Chemical Reviews, 2015

Publication

&lt;1 %

---

Exclude quotes      On

Exclude matches      Off

Exclude bibliography      On

# Potential Molecular Interaction of Nutmeg's Myristica fragrans Active Compound via Activation of Caspase-3

---

GRADEMARK REPORT

---

FINAL GRADE

**/100**

GENERAL COMMENTS

**Instructor**

---

PAGE 1

---

PAGE 2

---

PAGE 3

---

PAGE 4

---

PAGE 5

---

PAGE 6

---

PAGE 7

---

PAGE 8

---

PAGE 9

---

PAGE 10

---

PAGE 11

---

PAGE 12

---