



## 3D PHARMACOPHORE VIRTUAL SCREENING OF INDONESIA'S MEDICINAL PLANTS DATABASE FOR SIRT1 ACTIVATOR

Oleh:

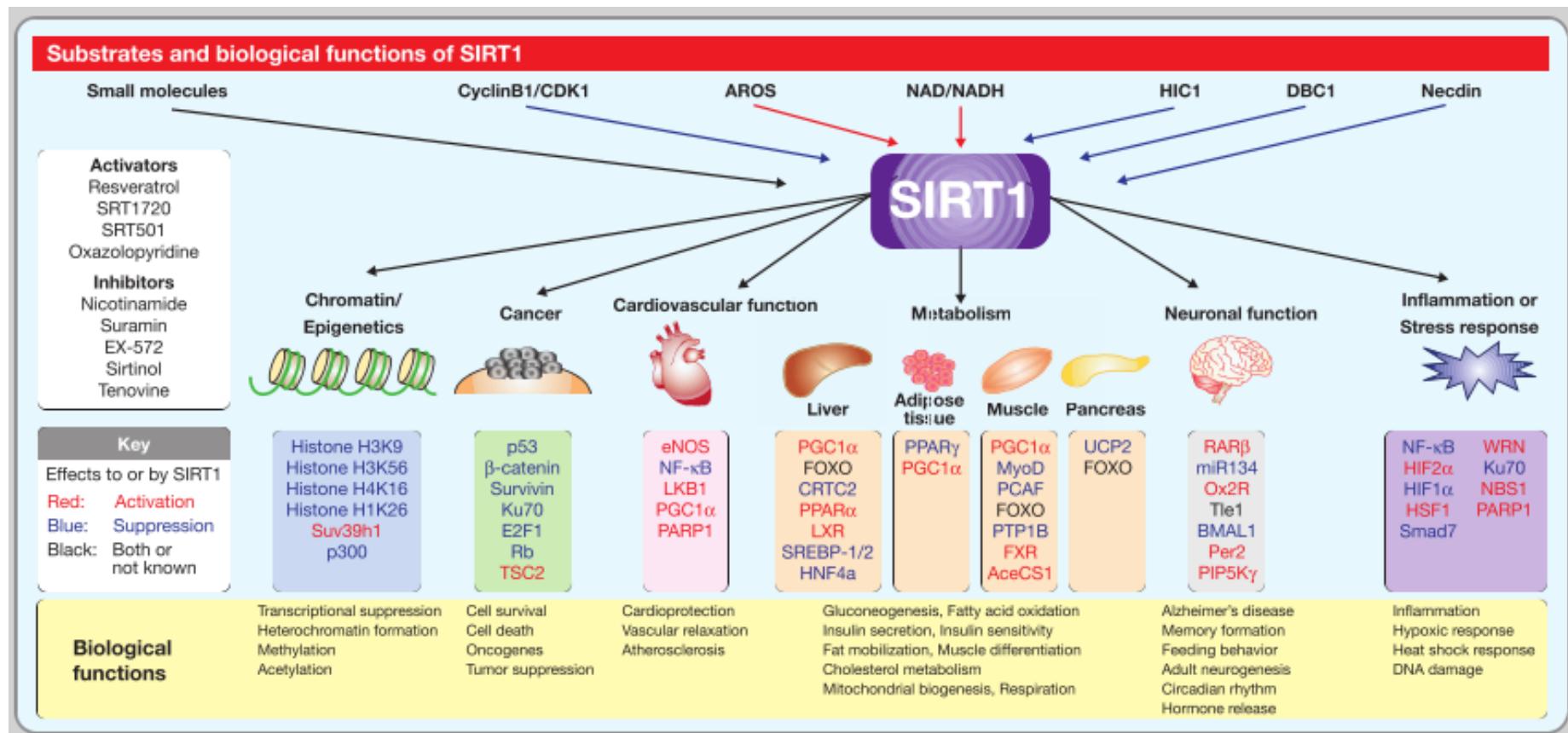
Azminah, Linda Erlina, Andika and Arry Yanuar\*

Faculty of Pharmacy, University of Indonesia

Email Corresponding Author (\*): [arry.yanuar@ui.ac.id](mailto:arry.yanuar@ui.ac.id)

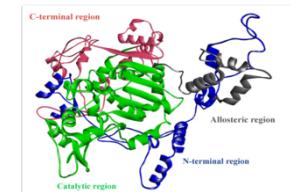
The 7 th International Conference On Advanced Computer Science and Information System (ICACCSIS), October 7-9 th 2015 Faculty of Computer Science Universitas Indonesia. Depok Indonesia

# SIRT1 activator has been implicated in diseases such as type II diabetes, inflammation, regulating aging process

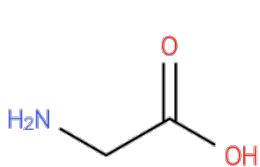


# SIRT1 is a nicotinamide adenine dinucleotide (NAD)<sup>+</sup>-dependent deacetylase of 747 residues (amino acid) (isoform UniProt accession code Q96EB6)

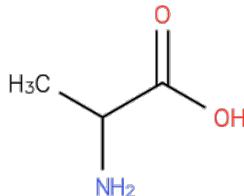
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VPAARGCPGAAAAAALWREAEAEAAAAGGEQEAQATAAAGEGEDNGPGLQGPSREPPLA  
DNLYDEDDDDEGEEEEAAAAAIGYRDNLLFGDEIITNGFHSCESDEEDRASHASSSDWT  
PRPRIGPYTFVQQHLMIGTDPRTILKDLLPETIPPPELDDMTLWQIVINILSEPPKRKKRKDI  
NTIEDAVKLLQECKKIIVLTGAGVS VSCGIPDFRSRDGIYARLA VDFPDLPDPQAMFDIEYF  
RKDPRPFFKFAKEIYPGQFQPSLCHKFIALSDKEGKLLRNYTQNIDTLEQVAGIQRIIQCHGS  
FATASCLICKYKV DCEAVRGDIFNQVVPRCP RCPA DEPLAIMKPEIVFFGENLPEQFHRAM  
KYDKDEV DLLIVIGSSLKVRPVALIPSSIPHEVPQILINREPLPHLHF DVELLGDCDV IINELCH  
RLGGEYAKLCCNPVKLSEITEKPPRTQKELAYLSELPP TPLHVSEDSSSPERTSPPDSSVIVTL  
LDQA AKSNDDLDVSES KGCMEEKPQEVQTSRNVESIAEQMENPDLKNVGSTGEKNERTS  
VAGTVRK CWP NRVAKEQISRR LDGNQYLFLPPNRYIFHGAEVY SDSE DDVLSSSSCGSNS  
DSGTCQSPSLEEP MEDESEIEFY NGLEDEPDVPERAGGAGFGTDGDDQEAINEAISVKQ  
EVTDMN YPSNKS



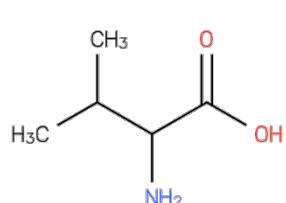
# Amino acid



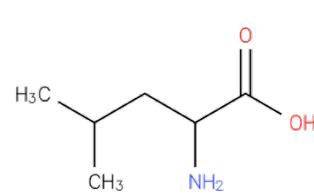
Glycine **G**



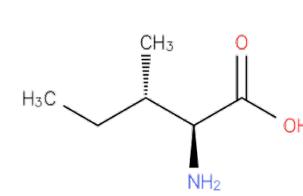
Alanine **A**



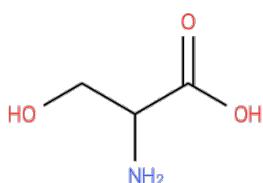
Valine **V**



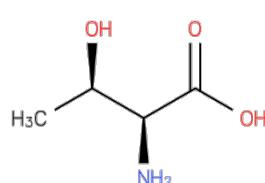
Leucine **L**



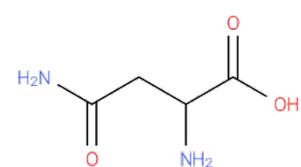
Isoleucine **I**



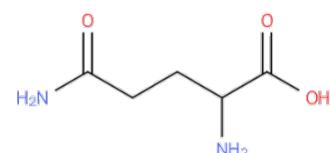
Serine **S**



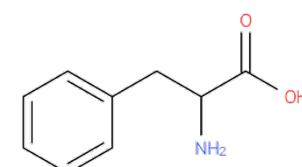
Threonine **T**



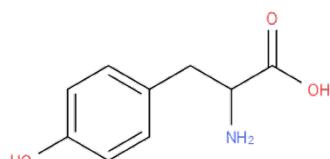
Asparagine **N**



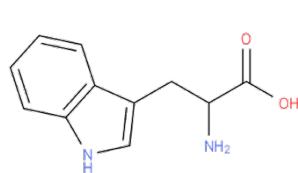
Glutamine **Q**



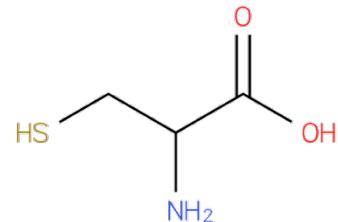
Phenylalanine **F**



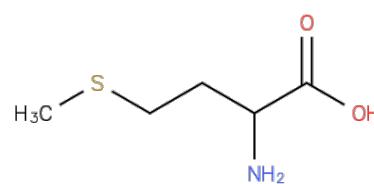
Tyrosine **Y**



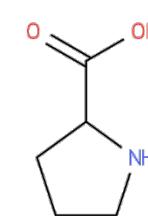
Tryptophan **W**



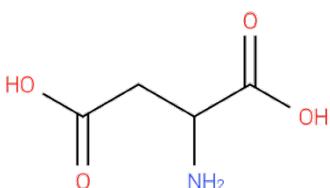
Cysteine **C**



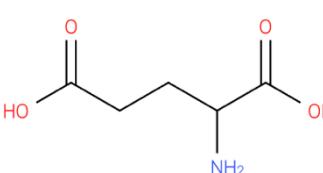
Methionine **M**



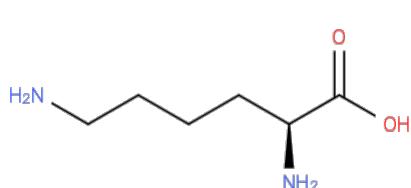
Proline **P**



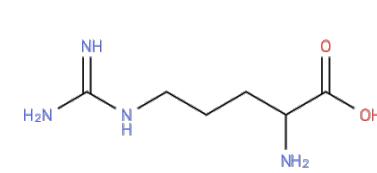
Aspartic acid **D**



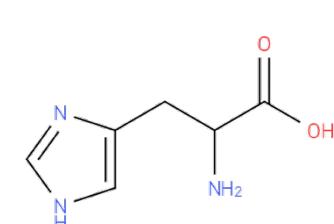
Glutamic acid **E**



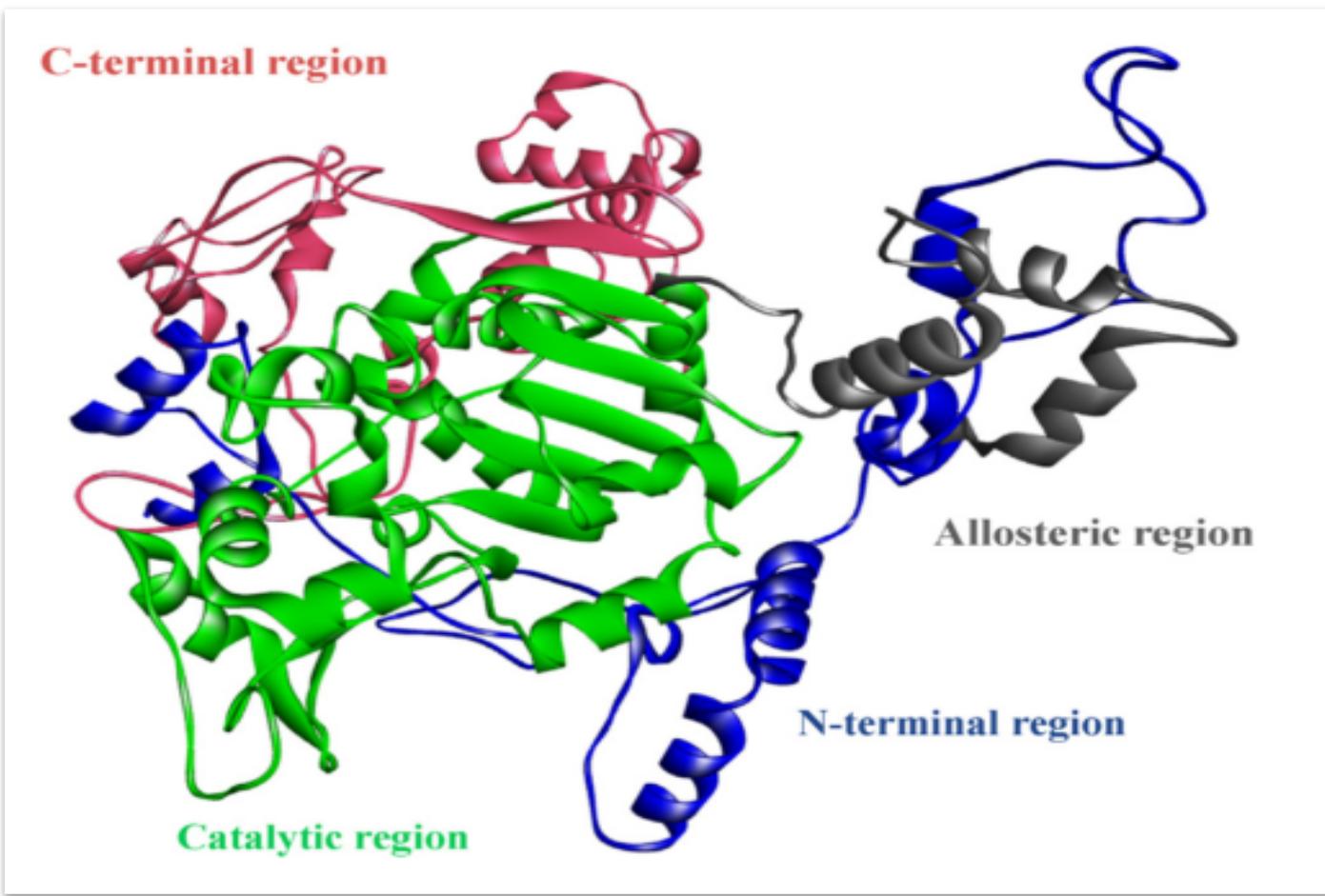
Lysine **K**



Arginine **R**



Histidine **H**



*Human SIRT1 modeled structure.  
N-terminal region (1-180), allosteric region (181-243),  
the catalytic site (244-512), the C-terminal region (513-747).*

# 3D Pharmacophore model developed with the help of LigandScout

create pharmacophore with LigandScout software



A 3-D pharmacophore concept is based on specifically those kinds of interactions that have been observed in drug-receptor interaction: hydrogen bonding (hydrogen bond acceptor [HBA], hydrogen bond donor [HBD] ), charge transfer, electrostatic, and hydrophobic interactions.

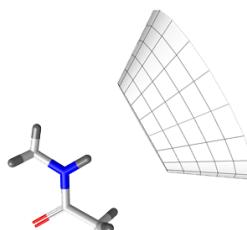
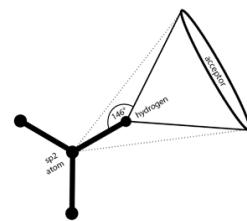


Figure 5.1. Rigid H-bonds constraint of an  $sp^2$  hybridized amide nitrogen.

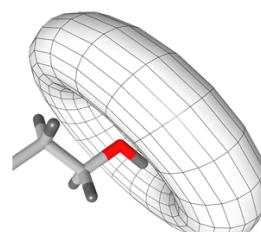
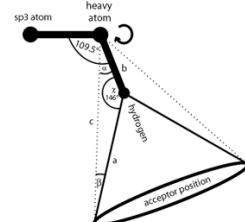


Figure 5.2. Flexible H-bonding constraint of an  $sp^3$  hybridized hydroxy group.

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LigandScout

ilb diverse

PharmacophoreDB

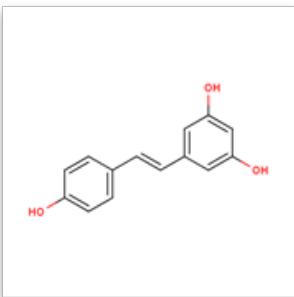
# In This study, virtual screening approach against Medicinal plants database

<http://herbaldb.farmasi.ui.ac.id>

The screenshot shows a web browser displaying the homepage of the Basis Data Tanaman Obat Indonesia (Basis Data Herbs Database) at <http://herbaldb.farmasi.ui.ac.id/v3/>. The title "BASIS DATA TANAMAN OBAT INDONESIA" is prominently displayed in white on a red header bar. Below the header is a black navigation bar with links: Beranda, Daftar Spesies, Daftar Senyawa, FAQs, Tentang Kami, IND, and ENG. On the left side, there is a yellow sidebar containing a search interface titled "Box of Search" with fields for "Kategori Pencarian" and "Kunci Pencarian", and a "Search" button. At the bottom of the sidebar is a "Members Login" section with a user icon. The main content area features a large image of an avocado tree with green leaves and fruit. To the right of the image, the text "Database Senyawa Aktif Tanaman Obat Indonesia" is displayed above the image. Below the image, the text "Avocado (Alpukat)" is shown, followed by a detailed description: "Tumbuhan Avocado berasal dari Meksiko dan Amerika Tengah dan kini banyak dibudidayakan di Amerika Selatan dan Amerika Tengah sebagai tanaman perkebunan monokultur dan sebagai tanaman pekarangan di daerah-daerah tropika lainnya di dunia."

# Resveratrol

Pharmacophore-base



*virtual screening approach against Medicinal plants database was used to find active compounds that have similarity pharmacophore features with **resveratrol** for SIRT activator (PDB ID 5BTR)*



## Computational details:

*Mac mini (late 2014),*

*Processor 2.6 Ghz Intel Core i5,*

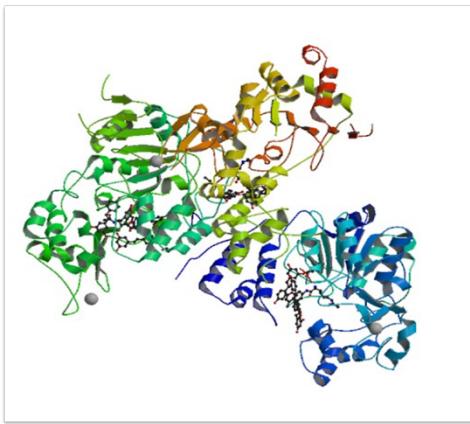
*Memory 8 GB 1600 MHz DDR3,*

*Graphics Intel Iris 1536 MB.*

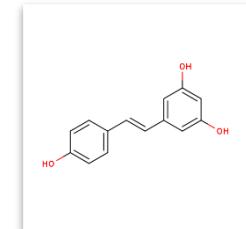


# WORK SCHEME

Download PDB file 5BTR in [www.pdb.com](http://www.pdb.com)

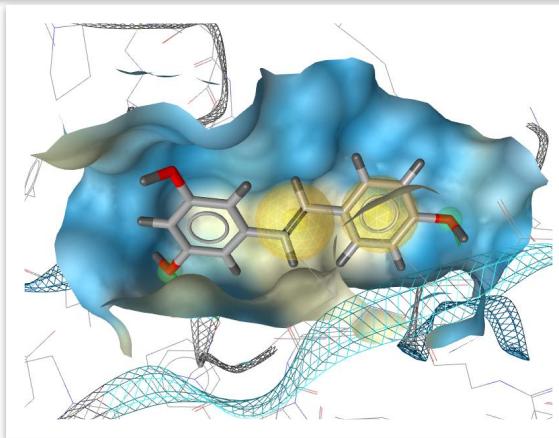
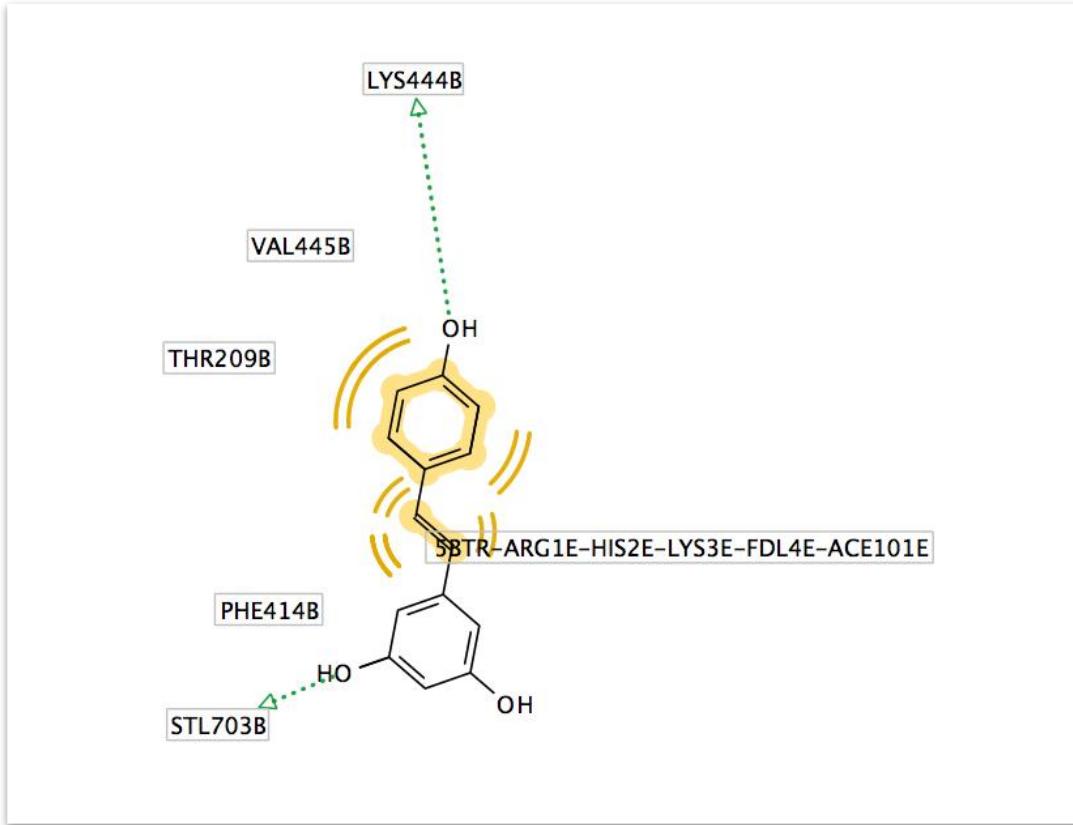


*create pharmacophore with:  
LigandScout software  
B\_STL702  
B\_STL703  
E\_STL102  
\*STL = Resveratrol*

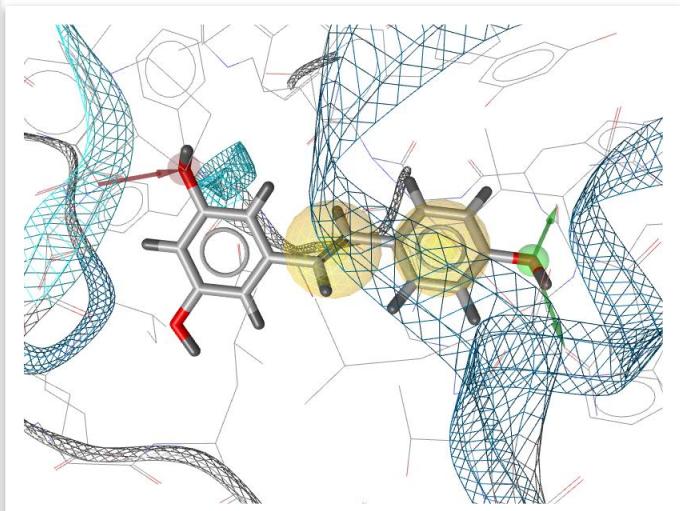
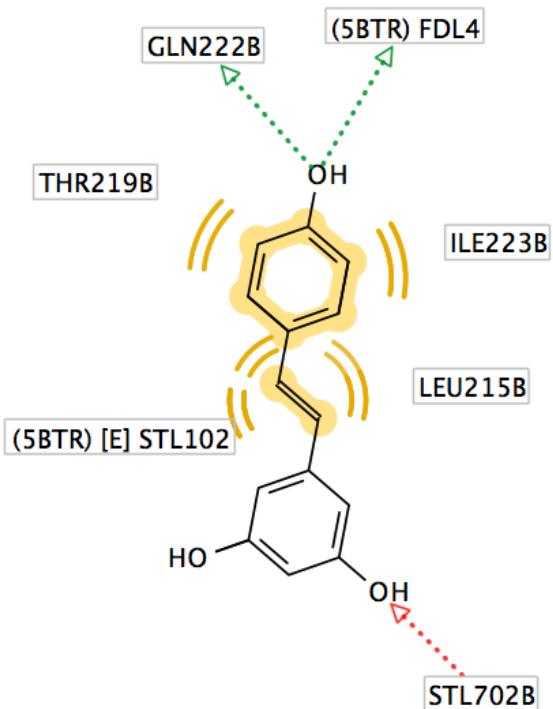


virtual screening approach against Medicinal plants database  
<http://herbaldb.farmasi.ui.ac.id> (HerbalBD\_best.ldb)  
1377 compounds  
screen with LigandScout software

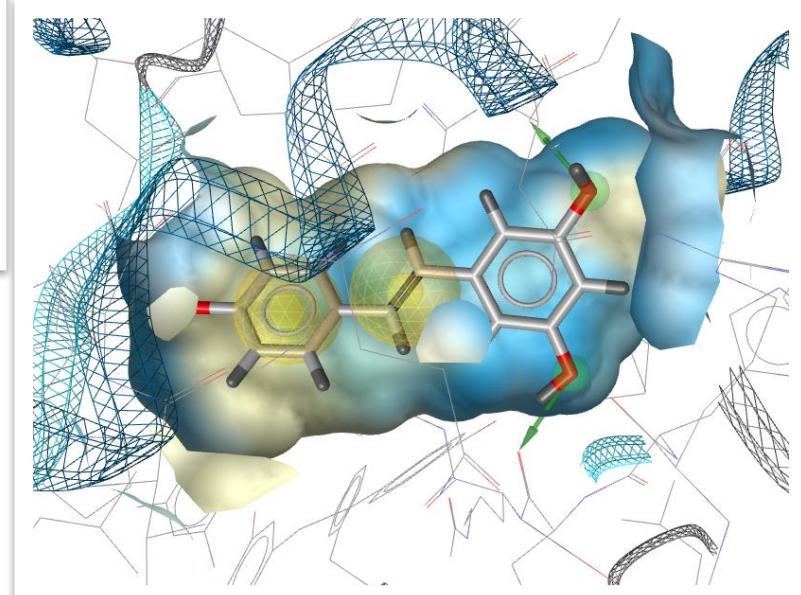
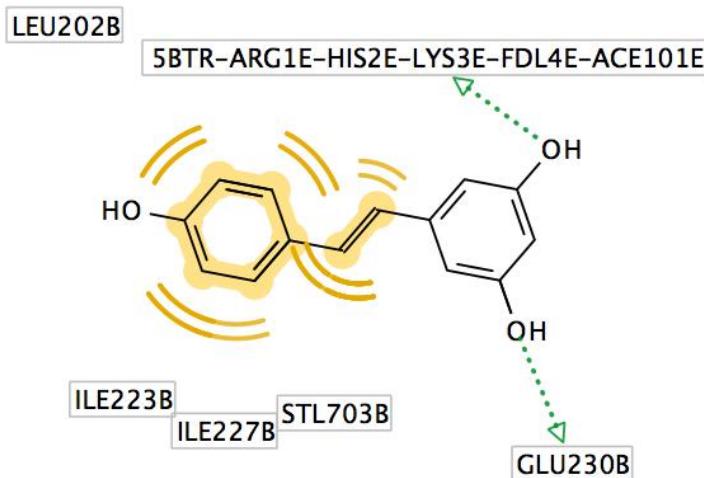
# 5BTR\_BSTL702



# 5BTR\_BSTL703



# 5BTR\_ESTL102



# 5BTR\_BSTL702

Name	Source Database	Pharmacophore-Fit Score
Antheraxanthin.mol	HerbalBD_best.ldb	46,06
trans-p-Ferulyl alcohol 4-O-[6-(2-methyl-3-hydroxypropionyl)]glucopyranoside.mol	HerbalBD_best.ldb	46,32

← → C 🌐 [heraldb.farmasi.ui.ac.id/v3/index.php?v=search](http://heraldb.farmasi.ui.ac.id/v3/index.php?v=search)

## BASIS DATA TANAMAN OBAT INDONESIA

Beranda Daftar Spesies Daftar Senyawa FAQs Tentang Kami IND ENG

**Box of Search**

Kategori Pencarian  
Senyawa Konci Pencarian  
antheraxanthin

Hasil Pencarian (Banyak baris data = 1)

No.	Senyawa	Knapsack ID	Metabolite ID	Pubchem ID	Spesies
1.	Antheraxanthin	C00003760	M00003760	5281223	1. <a href="#">Capsicum Annum</a> 2. <a href="#">Carica Papaya</a>

heraldb.farmasi.ui.ac.id/v3/popdetails\_content.php?con\_id=317

### Antheraxanthin | Daftar Spesies Yang Mengandung Antheraxanthin

No.	Spesies
1.	<a href="#">K0000055</a>   Capsicum Annum
2.	<a href="#">K0000037</a>   Carica Papaya

input word = C00011173

Metabolite Information				Structural formula
Name	trans-p-Ferulyl alcohol 4-O-[6-(2-methyl-3-hydroxypropionyl)] glucopyranoside			
Formula	C <sub>20</sub> H <sub>28</sub> O <sub>10</sub>			
Mw	428.16824712			
CAS RN	613232-82-9			
C_ID	C00011173 			
Organism	Kingdom	Family	Species	Reference
	Plantae	Solanaceae	Capsicum annuum	<a href="#">Ref.</a>



# 5BTR\_BSTL702

Name	Source Database	Pharmacophore-Fit Score
Fragransol A.mol	HerbalBD_best.ldb	57,42
Quercetin 3-(6"-malonylneohesperidoside).mol	HerbalBD_best.ldb	57,15
Fragransin D3.mol	HerbalBD_best.ldb	57,07
Fragransin C3b.mol	HerbalBD_best.ldb	56,75
Angolensin.mol	HerbalBD_best.ldb	56,74
Epicatechin-(4beta-8)-ent-epicatechin.mol	HerbalBD_best.ldb	56,55
Artocarpin.mol	HerbalBD_best.ldb	56,5
Kaempferol 3-glucosyl-(1-3)-rhamnosyl-(1-6)-galactoside.mol	HerbalBD_best.ldb	56,43
Mulberrin.mol	HerbalBD_best.ldb	56,11
Isookaninrhamnoside.mol	HerbalBD_best.ldb	56,02
Kuwanon T.mol	HerbalBD_best.ldb	55,96
trans-p-Ferulyl alcohol 4-O-[6-(2-methyl-3-hydroxypropionyl)] glucopyranoside.mol	HerbalBD_best.ldb	55,79
Kuwanone G.mol	HerbalBD_best.ldb	55,78
Eriodictin.mol	HerbalBD_best.ldb	55,59
Dihydroguaiaretic acid.mol	HerbalBD_best.ldb	55,52
Sanggenofuran A.mol	HerbalBD_best.ldb	55,43
15-HETE.mol	HerbalBD_best.ldb	55,24
Marmin.mol	HerbalBD_best.ldb	55,18

# BASIS DATA TANAMAN OBAT INDONESIA

Beranda Daftar Spesies Daftar Senyawa FAQs Tentang Kami IND ENG

**Box of Search**

Kategori Pencarian  
Senyawa ▼

Kunci Pencarian  
fragransol A

Search

## Hasil Pencarian (Banyak baris data = 1)

No.	Senyawa	Knapsack ID	Metabolite ID	Pubchem ID	Spesies
1.	<a href="#">Fragransol A</a>	C00024174	M00024174		1. <a href="#">Myristica Fragrans</a>



## 5BTR\_ESTL102

Name	Source Database	Pharmacophore-Fit Score
trans-p-Feruloyl-beta-D-glucopyranoside.mol	HerbalBD_best.ldb	47,58
Orientanol D.mol	HerbalBD_best.ldb	47,08
Artonin D.mol	HerbalBD_best.ldb	47,02
Gambiriin B1.mol	HerbalBD_best.ldb	46,6
Mulberrin.mol	HerbalBD_best.ldb	46,52
Artocarpin.mol	HerbalBD_best.ldb	46,52
Kuwanon T.mol	HerbalBD_best.ldb	46,51
Heterophyllin.mol	HerbalBD_best.ldb	46,47
Nirurin.mol	HerbalBD_best.ldb	46,25
Tectograndinol.mol	HerbalBD_best.ldb	46,21
Floweron.mol	HerbalBD_best.ldb	46,19
Safynol.mol	HerbalBD_best.ldb	46,11
3-Methylpentyl glucosinolate.mol	HerbalBD_best.ldb	45,8
Lutein.mol	HerbalBD_best.ldb	45,75
Dehydrosafynol.mol	HerbalBD_best.ldb	45,62

# BASIS DATA TANAMAN OBAT INDONESIA

Beranda Daftar Spesies Daftar Senyawa FAQs Tentang Kami IND ENG

**Box of Search**

Kategori Pencarian  
Senyawa ▼

Kunci Pencarian  
Orientanol D

**Search**

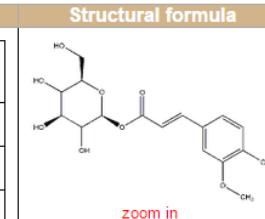
## Hasil Pencarian (Banyak baris data = 1)

No.	Senyawa	Knapsack ID	Metabolite ID	Pubchem ID	Spesies
1.	<a href="#">Orientanol D</a>	C00018982	M00018982		1. <a href="#">Erythrina Orientalis</a>



Input word = [C00037931](#)

Metabolite Information	
Name	trans-p-Feruloyl beta-D-glucopyranoside (-)-trans-p-Feruloyl beta-D-glucopyranoside
Formula	C16H20O9
Mw	356.11073224
CAS RN	64625-37-2
C_ID	<a href="#">C00037931</a> 3D
Organism	Kingdom Family Species Reference
	Plantae Solanaceae Capsicum annum L. Ref.



# Conclusions



virtual screening approach against Medicinal plants database <http://herbaldb.farmasi.ui.ac.id> was used to find active compounds that have similarity pharmacophore features with resveratrol for SIRT activator (PDB ID 5BTR)

**B\_STL702  
2 HIT**

Name	Source Database	Pharmacophore-Fit Score
Antheraxanthin.mol	HerbalBD_best.lbd	46,06
trans-p-Ferulyl alcohol 4-O-[6-(2-methyl-3-hydroxypropionyl)]glucopyranoside.mol	HerbalBD_best.lbd	46,32

**B\_STL703  
18 HIT**

Name	Source Database	Pharmacophore-Fit Score
Fragransol A.mol	HerbalBD_best.lbd	57,42
Quercetin 3-(6"-malonylneohesperidoside).mol	HerbalBD_best.lbd	57,15
Fragransin D3.mol	HerbalBD_best.lbd	57,07
Fragransin C3b.mol	HerbalBD_best.lbd	56,75
Angolensin.mol	HerbalBD_best.lbd	56,74
Epicatechin-(4beta-8)-ent-epicatechin.mol	HerbalBD_best.lbd	56,55
Artocarpin.mol	HerbalBD_best.lbd	56,5
Kaempferol 3-glucosyl-(1-3)-rhamnosyl-(1-6)-galactoside.mol	HerbalBD_best.lbd	56,43
Mulberrin.mol	HerbalBD_best.lbd	56,11
Isookaninrhamnoside.mol	HerbalBD_best.lbd	56,02
Kuwanon T.mol	HerbalBD_best.lbd	55,96
trans-p-Ferulyl alcohol 4-O-[6-(2-methyl-3-hydroxypropionyl)] glucopyranoside.mol	HerbalBD_best.lbd	55,79
Kuwanone G.mol	HerbalBD_best.lbd	55,78
Eriodictin.mol	HerbalBD_best.lbd	55,59
Dihydroguaiaretic acid.mol	HerbalBD_best.lbd	55,52
Sanggenofuran A.mol	HerbalBD_best.lbd	55,43
15-HETE.mol	HerbalBD_best.lbd	55,24
Marmin.mol	HerbalBD_best.lbd	55,18

**E\_STL102  
15 HIT**

Name	Source Database	Pharmacophore-Fit Score
trans-p-Feruloyl-beta-D-glucopyranoside.mol	HerbalBD_best.lbd	47,58
Orientanol D.mol	HerbalBD_best.lbd	47,08
Artonin D.mol	HerbalBD_best.lbd	47,02
Gambirin B1.mol	HerbalBD_best.lbd	46,6
Mulberrin.mol	HerbalBD_best.lbd	46,52
Artocarpin.mol	HerbalBD_best.lbd	46,52
Kuwanon T.mol	HerbalBD_best.lbd	46,51
Heterophyllin.mol	HerbalBD_best.lbd	46,47
Nirurin.mol	HerbalBD_best.lbd	46,25
Tectograndinol.mol	HerbalBD_best.lbd	46,21
Floweron.mol	HerbalBD_best.lbd	46,19
Safynol.mol	HerbalBD_best.lbd	46,11
3-Methylpentyl glucosinolate.mol	HerbalBD_best.lbd	45,8
Lutein.mol	HerbalBD_best.lbd	45,75
Dehydrosafynol.mol	HerbalBD_best.lbd	45,62

**THANK YOU**



The 7 th International Conference On Advanced  
Computer Science and Information System (ICACCSIS),  
October 7-9 th 2015 Faculty of Computer Science  
Universitas Indonesia.  
Depok Indonesia

**Dr. Arry Yanuar\***  
and  
**Linda Erlina, Andika**



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Box of Search

Kategori Pencarian:   
Kunci Pencarian:  Search

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Database Senyawa Aktif Tanaman Obat Indonesia

**Avocado (Alpukat)**  
Tumbuhan Avocado berasal dari Meksiko dan Amerika Tengah dan kini banyak dibudidayakan di Amerika Selatan dan Amerika Tengah sebagai tanaman perkebunan monokultur dan sebagai tanaman pekarangan di daerah-daerah tropika lainnya di dunia.

Thierry Langer, CEO of [Prestwick Chemical](#)