

## Supplementary data

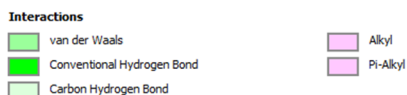
**Table S1.** Complete list of rooibos compounds investigated and details of Lipinski's violation

S/N	Compounds	Passed Lipinski's/ no of violations	The 13 compounds
1	(+)-catechin	Yes	1
2	Apigenin	Yes	2
3	Aspalathin	No - 2	
4	Carlinoside	No - 3	
5	Chlorogenic acid	Yes - 1	3
6	Chrysoeriol	Yes	4
7	Dihydrochalcone	Yes	5
8	Eriodictyol 5,3'-di-O-glucoside	No - 3	
9	Esculin	Yes	6
10	Ferulic	Yes	7
11	Hyperoside	No - 2	
12	Isocarlinoside	No - 3	
13	Isoorientin	No - 2	
14	Isoquercitrin	No - 2	
15	Isovitexin	Yes	8
16	Kaempferol	Yes	9
17	Luteolin	No - 2	
18	Luteolin-7-O-glucoside	No - 2	
19	Neocarlinoside	No - 3	
20	Nothofagin	Yes - 1	10
21	Orientin	No - 2 violations	
22	Patuletin 7-glucoside	No - 2 violations	
23	<i>p</i> -coumaric acid	Yes	11
24	Procyanidin B3	No - 3	
25	Quercetin	No	
26	Quercetin-3- <i>O</i> -arabinoglucoside	No - 3	
27	Quercetin-3- <i>O</i> -galactoside	No - 2	
28	Quercetin-3- <i>O</i> -glucoside	No - 2	
29	Quercetin-3- <i>O</i> -robinobioside	No - 3	
30	Quercitrin	No - 2	
31	Rutin	No - 3	
32	Safflomin	No - 3	
33	Scoparin	No - 2	
34	Sinapic acid	Yes	12
35	Vicenin-2	No	
36	Vitexin	Yes - 1	13

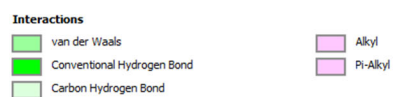
**Table S2.** 2D interactions of key targets and their associated key rooibos compounds in the HIF-1 pathway.

Compounds	2D interactions
EGFR	
Apigenin	60 ns
	<p>Interactions</p> <ul style="list-style-type: none"><li>van der Waals</li><li>Conventional Hydrogen Bond</li><li>Unfavorable Acceptor-Acceptor</li><li>Pi-Alkyl</li></ul>
	30 ns
	<p>Interactions</p> <ul style="list-style-type: none"><li>van der Waals</li><li>Conventional Hydrogen Bond</li><li>Carbon Hydrogen Bond</li><li>Pi-Sigma</li><li>Pi-Alkyl</li></ul>
	0 ns
	<p>Interactions</p> <ul style="list-style-type: none"><li>van der Waals</li><li>Conventional Hydrogen Bond</li><li>Pi-Alkyl</li></ul>

60 ns



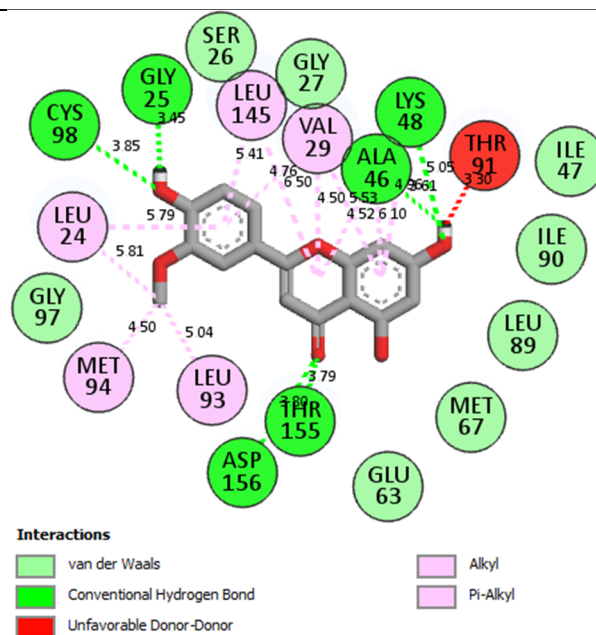
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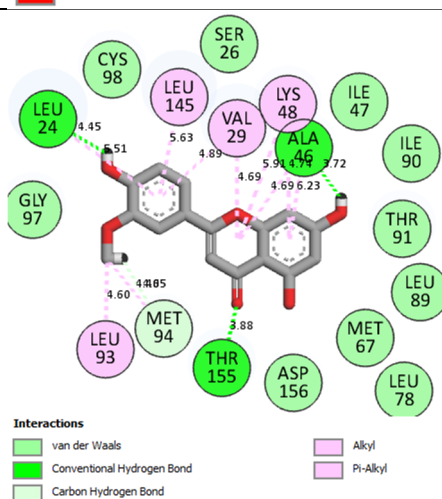
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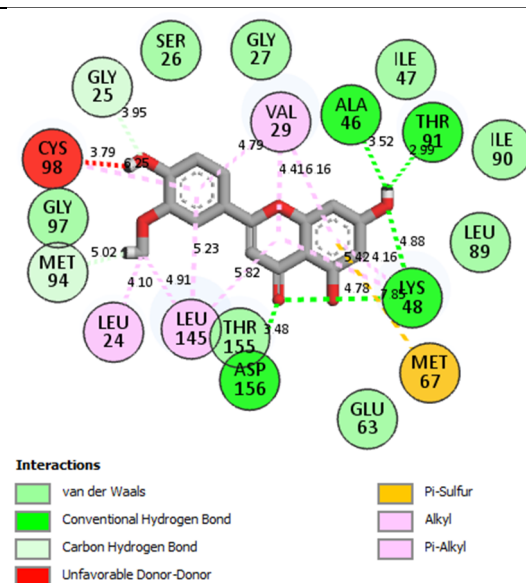
Chrysoeriol 60 ns



30 ns



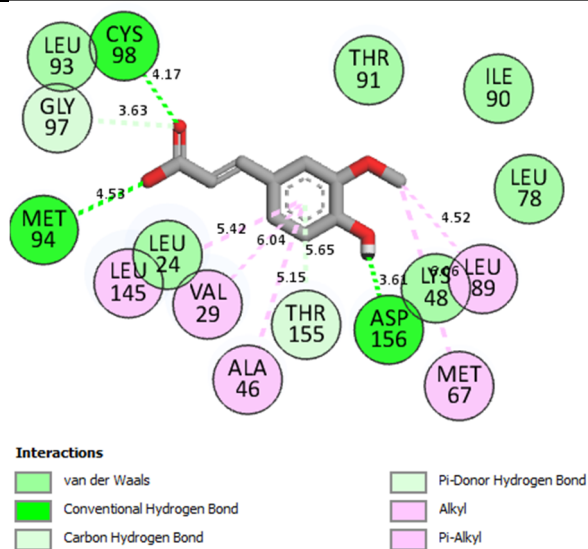
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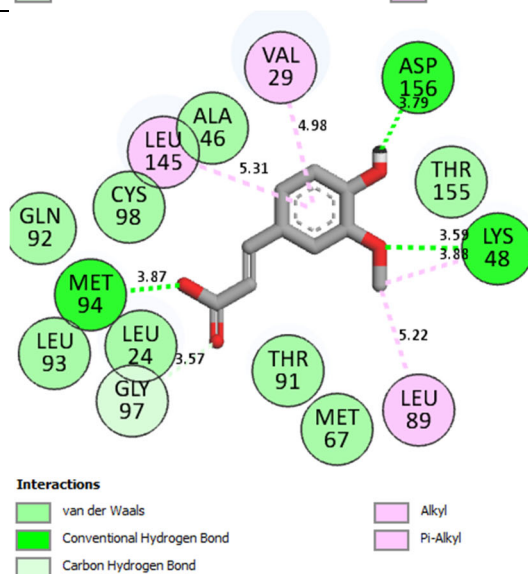


Ferulic

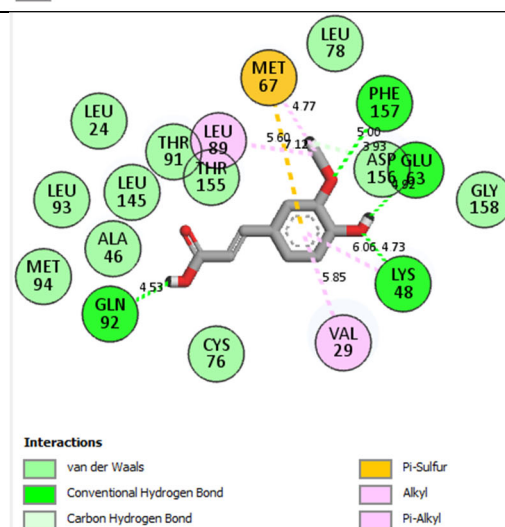
60 ns



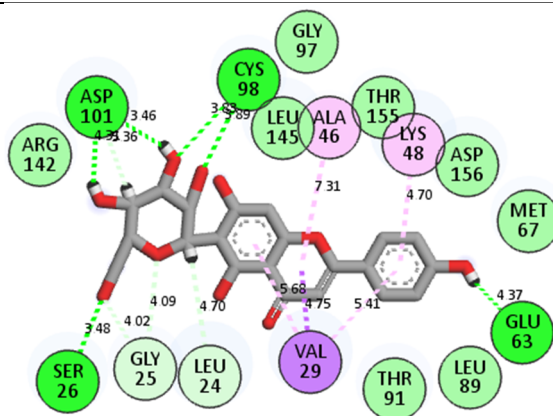
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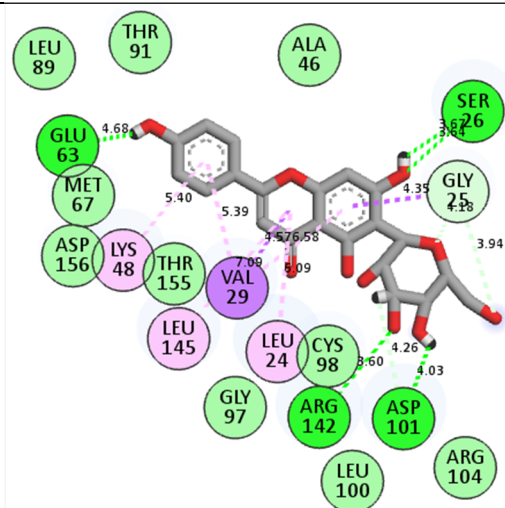
Isovitexin 60 ns



Interactions

- van der Waals
- Conventional Hydrogen Bond
- Carbon Hydrogen Bond
- Pi-Sigma
- Pi-Alkyl

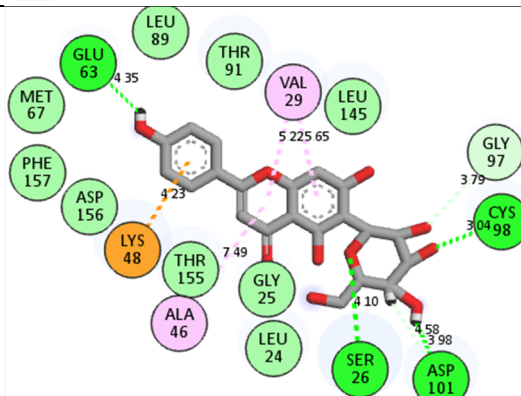
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Interactions

- van der Waals
- Conventional Hydrogen Bond
- Carbon Hydrogen Bond
- Pi-Sigma
- Pi-Alkyl

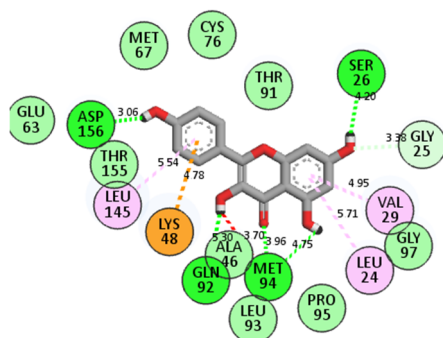
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Interactions

- van der Waals
- Conventional Hydrogen Bond
- Carbon Hydrogen Bond
- Pi-Cation
- Pi-Alkyl

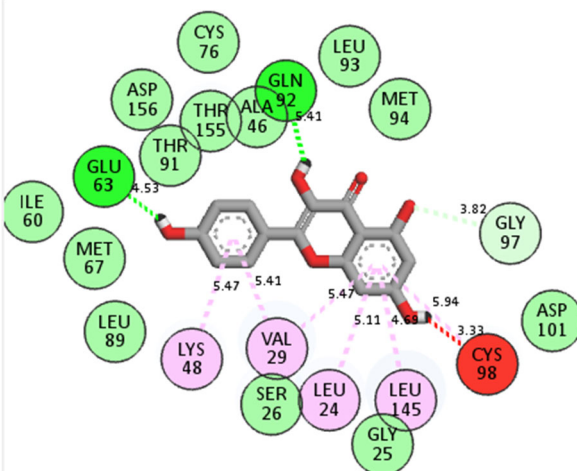
Kaempferol 60 ns



**Interactions**

- van der Waals
- Conventional Hydrogen Bond
- Carbon Hydrogen Bond
- Unfavorable Donor-Donor
- Pi-Cation
- Pi-Alkyl

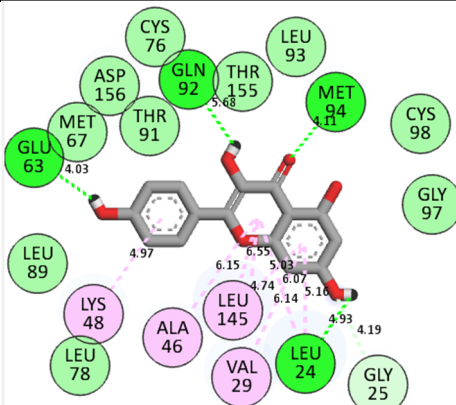
30 ns



**Interactions**

- van der Waals
- Conventional Hydrogen Bond
- Carbon Hydrogen Bond
- Unfavorable Donor-Donor
- Pi-Alkyl

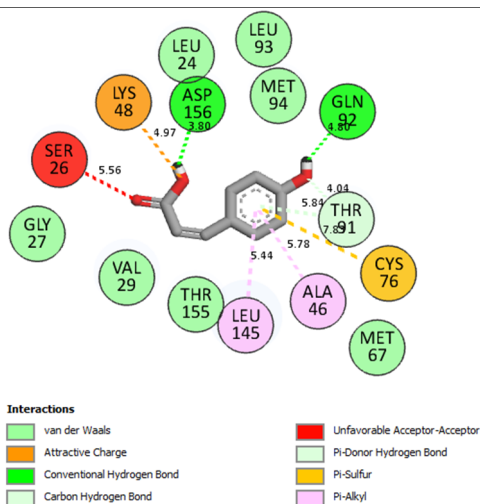
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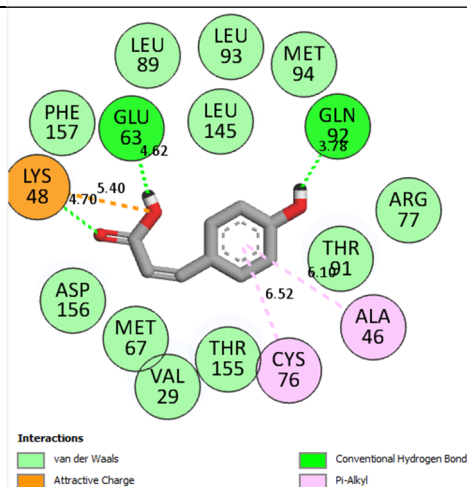
**Interactions**

- van der Waals
- Conventional Hydrogen Bond
- Carbon Hydrogen Bond
- Pi-Alkyl

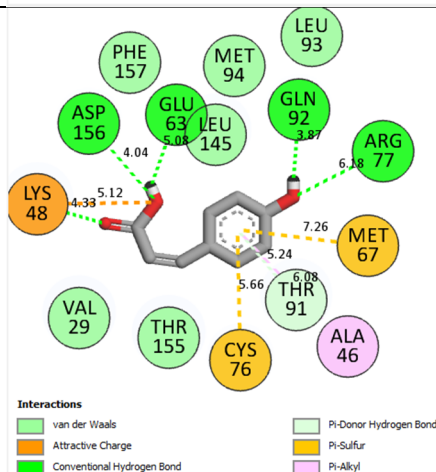
*P*-coumaric acid 60 ns



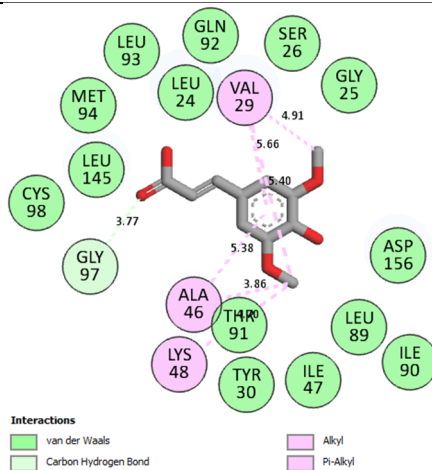
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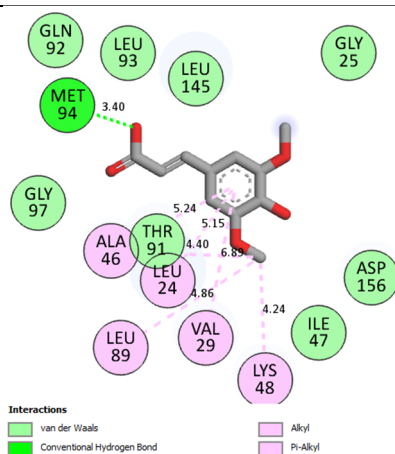
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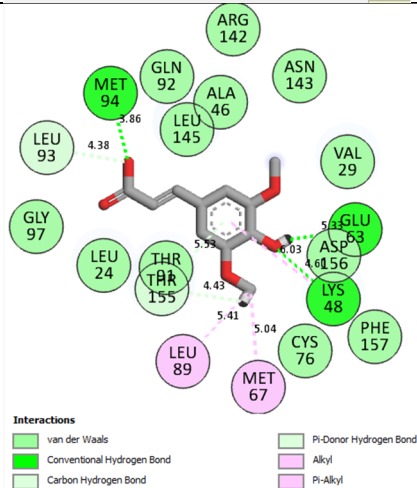
Sinapic acid 60 ns



30 ns

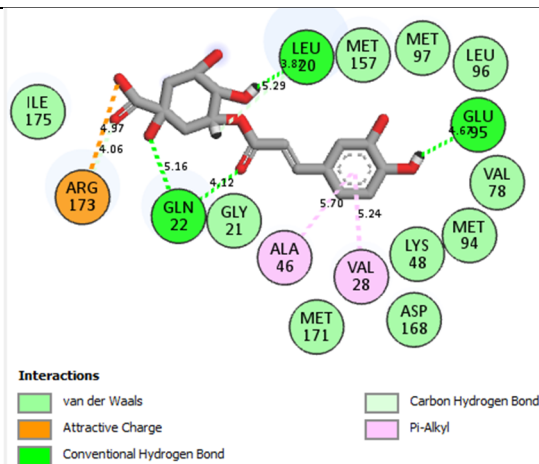


0 ns

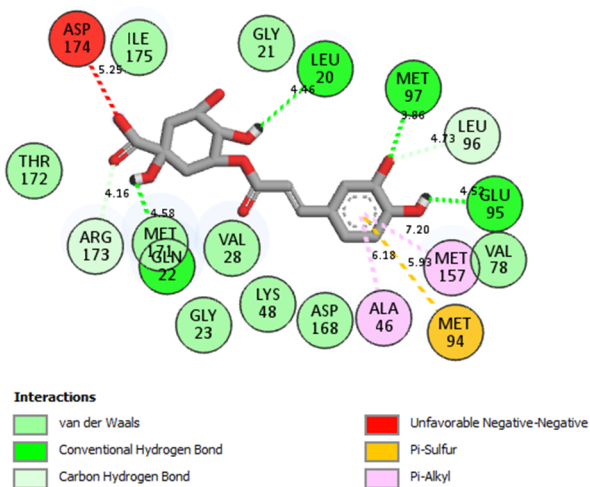


IGF1R

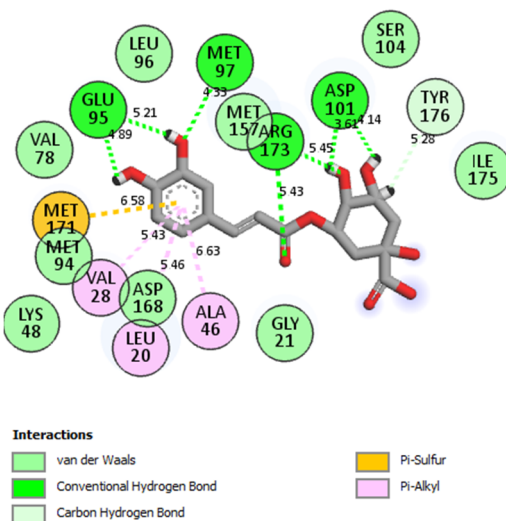
# Chlorogenic acid



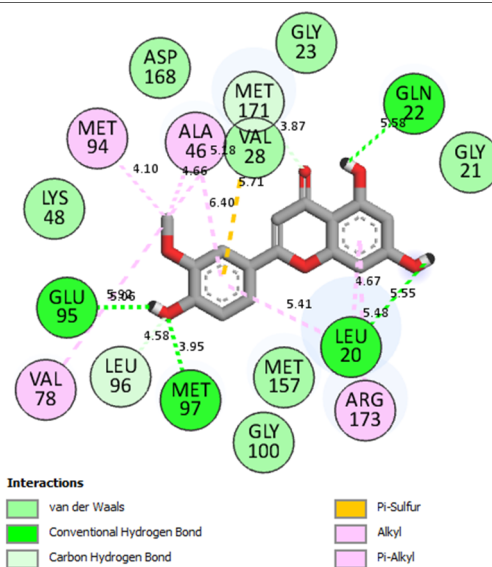
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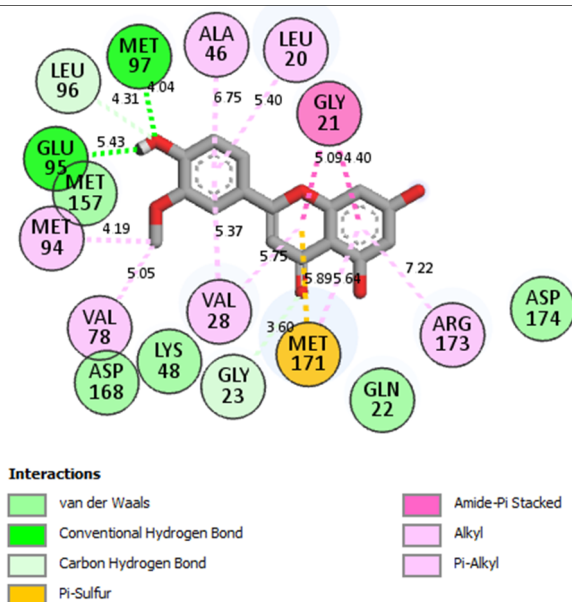
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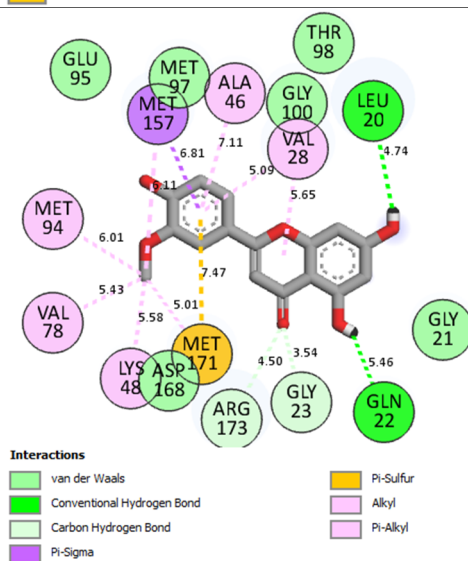
Chrysoeriol 60 ns



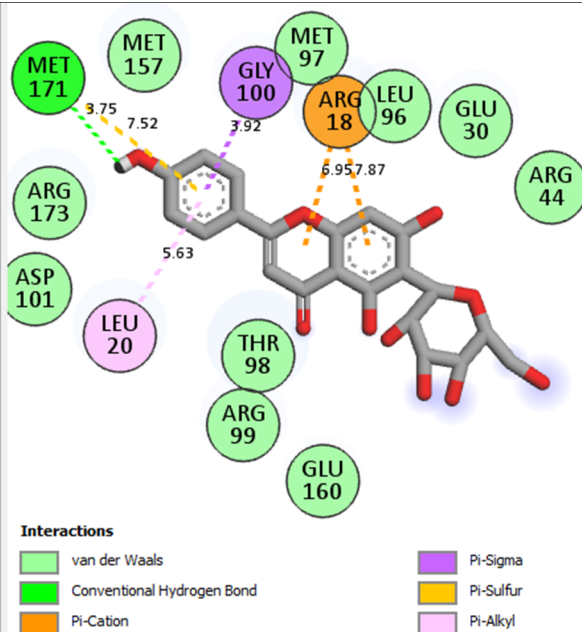
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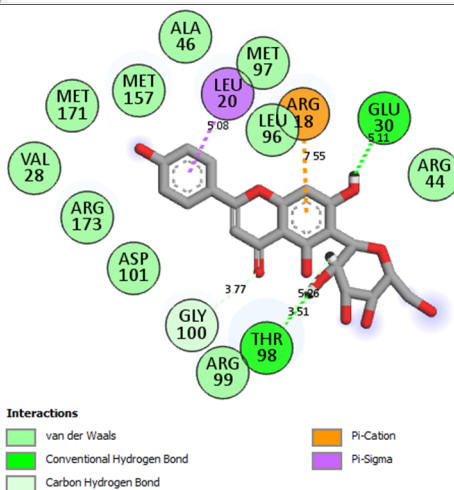
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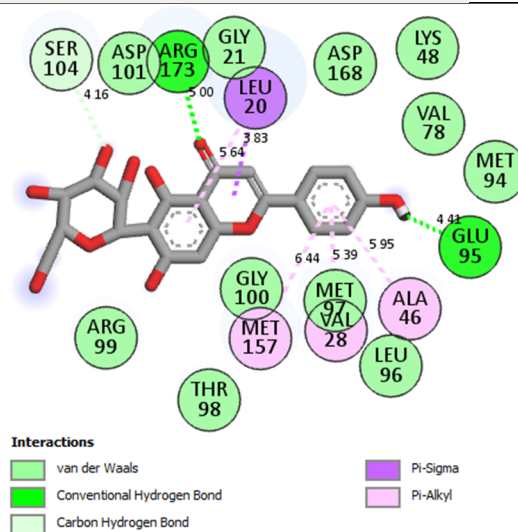
Isovitexin 60 ns



30 ns



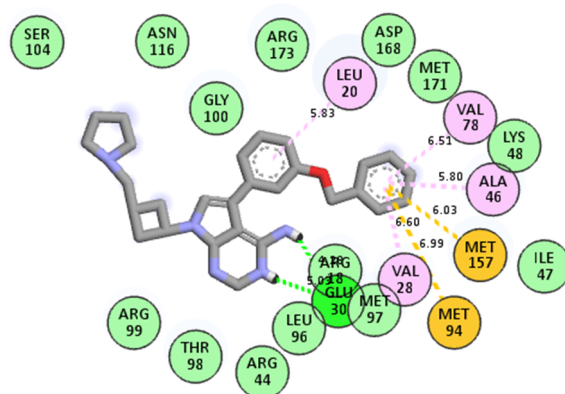
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NVP-  
ADW742

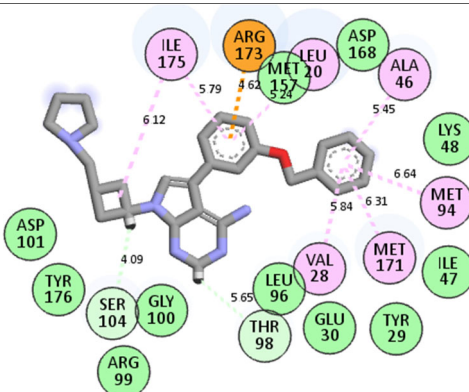
60 ns



Interactions

- van der Waals
- Conventional Hydrogen Bond
- Pi-Sulfur
- Pi-Alkyl

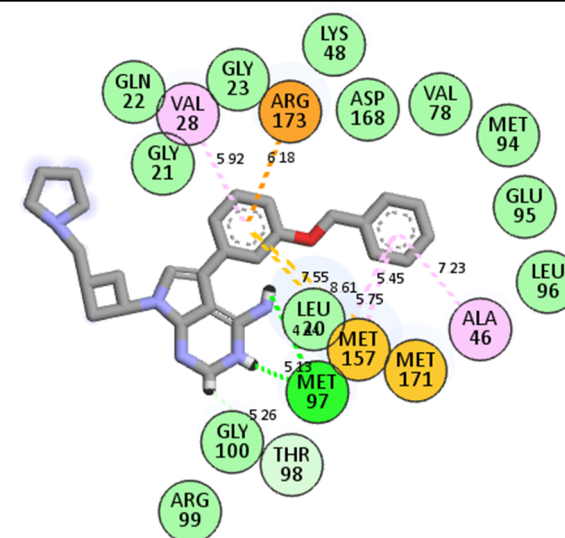
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Interactions

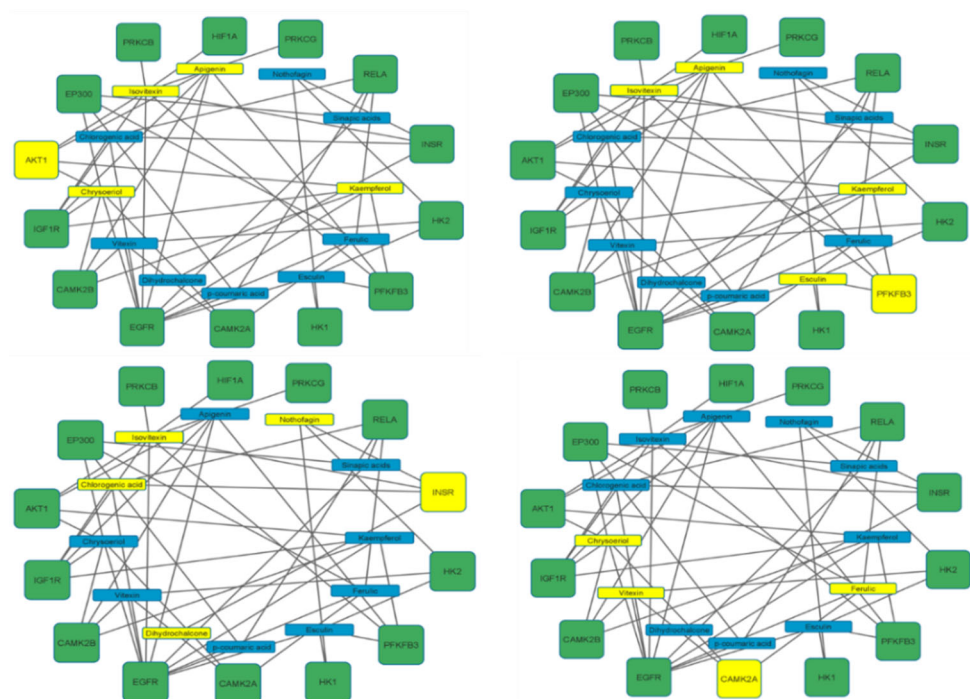
- van der Waals
- Carbon Hydrogen Bond
- Pi-Cation
- Alkyl
- Pi-Alkyl

0 ns



Interactions

- van der Waals
- Conventional Hydrogen Bond
- Carbon Hydrogen Bond
- Pi-Cation
- Pi-Sulfur
- Pi-Alkyl



**Figure S1.** Rooibos compounds (4, 4, 4 and 3, respectively) with good interactions linked to other genes (AKT1, PFKFB3, INSR and CAMPK2A) related to the HIF-1 signaling pathway.