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Exploring the Potential of *Saussurea Costus* Bioactive Compounds in Targeting MMP2/9 for Innovative Breast Cancer Therapy: An In-Silico Perspective

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Abstract:

Molecular docking studies further confirmed that bioactive compounds in *Saussurea costus* (COS), such as prop-2-enoate (LTS0119846), methyl acetate (LTS0188050), methyl acetate (LTS0102500), prop-2-enoate (LTS0147418), and oxane-3,4,5-triol (LTS0253995), interact with key metastasis-related proteins, including matrix metalloproteinase (MMP-2 and MMP-9), which contribute to its anti-metastatic effects. These findings suggest that COS bioactive compounds may be promising anticancer agents of natural origin. This study highlights the potential of COS as a natural therapeutic agent in cancer treatment, offering a multi-targeted approach that addresses both tumor progression and metastasis. The integration of COS into chemotherapy regimens could improve treatment outcomes. Future studies should focus on validating these results *in vivo*, clinical trials, and bioavailability optimization to facilitate the translation of COS-based therapies into clinical practice.

Keywords: *Saussurea costus*; Breast cancer; MMP2; MMP9; Molecular docking.

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1. Introduction

Cancer remains a significant challenge for global public health, accounting for nearly one in six deaths worldwide. Even with remarkable progress in cancer treatment in recent decades, the intricate nature of cancer cells, which facilitates swift mutation processes and reduces the effectiveness of standard chemotherapy, continues to fuel research into alternative and complementary therapy treatments (Sung et al. 2021). Breast cancer is the most common tumor among women worldwide, and it is a highly heterogeneous disease that demands specific therapeutic engagement focused on molecular profiling (Siegel et al. 2021).

Breast cancer is considered the most common type of cancer found in women. Today represents a significant challenge to public health (Masoud and Pagès 2017). Hormone receptors like estrogen or progesterone have been classified as estrogen receptor-positive or progesterone receptor-positive breast cancer, respectively, and human epidermal growth factor receptor-2-positive expressed cancer (Gluz et al. 2009; Murphy and Dickler 2016). The triple-negative breast cancer treatment remains a challenge due to its aggressive characteristics and limited therapy (Wang et al. 2018). Thus, in contemporary times, natural compounds are increasingly put under the scanner

for their potential anti-cancer propensities as they may be targeted and less-toxic agents than synthetic drugs (Newman and Cragg 2016; El-Far et al. 2025). Among promising medicinal plants, the anticancer potential of *Saussurea costus* (COS) draws attention. COS is commonly found in some parts of Asia and has been used for treating inflammatory diseases, liver diseases, and respiratory tract disorders in Ayurveda and other systems of medicine (Ali et al. 2021). It has been established recently that several bioactive components exist in COS, such as prop-2-enoate (LTS0119846), methyl acetate (LTS0188050), methyl acetate (LTS0102500), prop-2-enoate (LTS0147418), and oxane-3,4,5-triol (LTS0253995) that could potentially show anticancer efficacy (Hassan and Masoodi 2019). These compounds have been confirmed to restrict cancer cell growth, promote cancer cell programmed death, and interfere with cellular movement, thus placing COS as a candidate for advances in oncology (Ali et al. 2021).

Matrix metalloproteinases (MMPs), particularly MMP-2 and MMP-9, play a role in the unfolding processes of many cancers, including breast cancer. In all these studies, MMPs were named as mediators. COS has been shown to modulate these enzymes and thus prevent the spread of malignant transformation to the surrounding tissue (Chen, X., Zhao, Y., & Wang 2019).

Molecular docking is a computational method for predicting the preferential orientation of one molecule to a second molecule when they are bound together to form a stable complex (Khanna et al. 2018; Crampon et al. 2022) by simulating the binding interactions between a ligand (e.g., a bioactive compound from COS and a receptor protein (e.g., a target enzyme or protein), molecular docking can provide insights into the ligand's binding affinity, binding mode, and potential biological activity (Agu et al. 2023). Molecular docking offers valuable insights into potential drug-target interactions; it is essential to note that it is a computational process that requires experimental validation. Factors such as protein flexibility, solvent effects, and dynamic interactions can influence the accuracy of docking predictions (Ali, R., Al-Quraishy, S., & Dkhil 2020). Future research should combine computational approaches with experimental validation to confirm COS compounds' binding modes and biological activities. In addition, exploring the synergistic effects of multiple bioactive COS compounds could lead to developing more potent and effective therapeutic agents (Hu, S. 2019). Further research using *in vivo* models and clinical trials could clarify the exact mechanisms and efficacy of COS in combination therapy with DOX (Tacar et al. 2013; Chen, X., Zhao, Y., & Wang 2019; Hu, S. 2019).

2. Materials and Methods

The three-dimensional structures of MMP2 (ID: P08253) and MMP9 (ID: P14780) were retrieved from the UniProt (https://www.uniprot.org/) database. Also, the three-dimensional structures of the main active ingredients of COS extract were retrieved from the LOTUS (https://lotus.naturalproducts.net/) database. Protein-ligand docking and virtualization were done using the 2015.10 (Vilar et al. 2008) software.

3. Results

Data represented in **Table 1** exhibited the Molecular docking interactions of *Saussurea costus* (COS) bioactive compounds against MMP2. [(2r,3s,4s,5r,6s)-6-{[(2s,3r,4s,5r,6r)-2-[(3-{[(2s,3r,4s,5r,6r)-6-({[(2r,3r,4s,5r,6s)-3,4-dihydroxy-6-methyl-5-{[(2s,3r,4s,5s,6r)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy}oxan-2-yl]oxy}methyl)-3,4,5-trihydroxy-oxan-2-yl]oxy}-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-7-yl)oxy]-5-hydroxy-6-(hydroxymethyl)-3-{[(2s,3r,4r,5r,6s)-3,4,5 -trihydroxy-6-methyloxan-2-yl]oxy}oxan-4-yl]oxy}-3,4,5-trihydroxyoxan-2-yl]methyl acetate (LTS0102500) exhibited the highest affinity to MMP2 binding site and interacted with it by binding free energy of -11.44 kcal/mol (**Figure 1**). While (6-{[2-({3-[(6-{[(3,4-dihydroxy-6-methyl-5-{[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy}oxan-2-yl)oxy]methyl}-3,4,5-trihydroxyoxan-2-yl)oxy]-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-7-yl}oxy)-5-hydroxy-6-(hydroxymethyl)-3-[(3,4,5-trihydroxy-6-methyloxan-2-yl)oxy]oxan-4-yl]oxy}-3,4,5-trihydroxyoxan-2-yl)methylacetate (LTS0188050) (**Figure 2**), (2s,3r,4r,5s,6s)-2-[(7-{[(2s,3r,4s,5r,6r)-4-{[(2s,3r,4s,5s,6r)-6-[(acetyloxy)methyl]-3,4,5-trihydroxyoxan-2-yl]oxy}-5-hydroxy-6-(hydroxymethyl)-3-{[(2s,3r,4r,5r, 6s)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxy}oxan-2-yl]oxy}-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-3-yl)oxy]-5-hydroxy-3-{[(2e)-3-(4-hydroxyphenyl) prop-2-enoyl]oxy}-6-methyloxan-4-yl(2e)-3-(4-hydroxyphenyl)prop-2-enoate (LTS0203744) (**Figure 3**), [6-({2-[(2-{3-[3-(acetyloxy)-5,5-

dimethylcyclopent-1-en-1-yl]-4-methoxyphenyl}-5,6-dihydroxy-4-oxochromen-7-yl)oxy]-5-hydroxy-6-(hydroxymethyl)-3-[(3,4,5-trihydroxy-6-methyloxan-2-yl)oxy]oxan-4-yl}oxy)-3,4,5-trihydroxyoxan-2-yl]methyl acetate (LTS0266101) (**Figure 4**), and [(2r,3s,4s,5r,6s)-6-{[(2s,3r,4s,5r,6r)-2-[(2-{3-[(3r)-3-(acetyloxy)-5,5-dimethylcyclopent-1-en-1-yl]-4-methoxyphenyl}-5,6-dihydroxy-4-oxochromen-7-yl)oxy]-5-hydroxy-6-(hydroxymethyl)-3-{[(2s,3r,4r,5r,6s)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxy}oxan-4-yl]oxy}-3,4,5-trihydroxyoxan-2-yl]methyl acetate (LTS0047986) (**Figure 5**) interacted with the binding site of MMP2 by binding free energies of -11.03, -11.02, 10.81, and -10.33 kcal/mol, respectively.

4. Discussion

Molecular docking studies provided valuable insights into the interaction between COS bioactive compounds (costunolide, dehydrocostus lactone, and vanillosmin) and MMPs. The binding affinities observed for these interactions support the hypothesis that COS inhibits MMP activity, thereby reducing extracellular matrix degradation and cancer cell invasion. Furthermore, COS's modulation of signaling pathways, such as NF-κB and PI3K/AKT/mTOR, adds another layer of complexity to its anti-cancer mechanisms (Kubczak et al. 2021). These findings align with studies on polyphenols like catechins and stilbenes, which also target these pathways to suppress tumor progression and enhance therapeutic outcomes (Newman and Cragg 2016).

In further confirmation, the molecular docking studies have demonstrated that COS bioactive components can interact with matrix metalloproteinases (MMP-2 and MMP-9), which connect cancer progression and metastasis via biochemical/cellular signals (McCawley and Matrisian 2000). COS constituents are thought to suppress metastasis and angiogenesis by inhibiting MMPs, particularly MMP-2 and MMP-9. MMPs are important in tumor metastasis since they facilitate the digestion of extracellular matrix components, making adjacent tissues accessible to cancer cells. Given that metastasis is one of the most common causes of cancer death, it is pertinent that COS may help mitigate the spread of breast cancer cells by inhibiting MMPs (McCawley and Matrisian 2000; Ashrafizadeh et al. 2020).

5. Conclusion

The Molecular docking interactions of *Saussurea costus* (COS) components such as prop-2-enoate (LTS0119846), methyl acetate (LTS0188050), methyl acetate (LTS0102500), prop-2-enoate (LTS0147418), and oxane-3,4,5-triol (LTS0253995) bioactive compounds show a high Binding free energy against MMP2 and MMP9 that significantly reduces cancer cell migration, and invasion.

This suggests a promising treatment strategy for both hormone receptor-positive and triple-negative breast cancers. The research also highlights the role of MMP2 and MMP9 in cancer progression.

The findings indicate that this approach could effectively target molecular pathways linked to cancer metastasis, although further studies are needed to explore these effects in detail.

Conflicts of Interest statement:

The authors have stated that there are no conflicts of interest.

Table 1. Molecular docking interactions of *Saussurea costus* (COS) bioactive compounds against matrix metallopeptidase 2 (MMP2)

Lotus ID	Binding free energy (kcal/mol)
LTS0102500	-11.44
LTS0188050	-11.03
LTS0203744	-11.02
LTS0266101	-10.81
LTS0047986	-10.33
LTS0119846	-10.05
LTS0245327	-9.93
LTS0147418	-9.63
LTS0016691	-9.32
LTS0253995	-9.15
LTS0083004	-9.10
LTS0051532	-8.44
LTS0134703	-8.19
LTS0226059	-7.85
LTS0158828	-7.82
LTS0111748	-7.44
LTS0201798	-7.40
LTS0198920	-7.29
LTS0078269	-7.20
LTS0274607	-7.15
LTS0241329	-7.05
LTS0093930	-6.91
LTS0126727	-6.90
LTS0023878	-6.72
LTS0134711	-6.69
LTS0037686	-6.64
LTS0235378	-6.61
LTS0085784	-6.59
LTS0201707	-6.46
LTS0141044	-6.43
LTS0086283	-6.39
LTS0154111	-6.39
LTS0207678	-6.35
LTS0182111	-6.34
LTS0079178	-6.31

Lotus ID	Binding free energy (kcal/mol)
LTS0046227	-6.26
LTS0116967	-6.26
LTS0148187	-6.26
LTS0174867	-6.24
LTS0046559	-6.24
LTS0256764	-6.22
LTS0042759	-6.21
LTS0210132	-6.18
LTS0272676	-6.18
LTS0246208	-6.15
LTS0127314	-6.10
LTS0222542	-6.09
LTS0264682	-6.02
LTS0272033	-6.00
LTS0220970	-5.98
LTS0079166	-5.96
LTS0108243	-5.96
LTS0027205	-5.94
LTS0115431	-5.90
LTS0135640	-5.89
LTS0172581	-5.89
LTS0201557	-5.87
LTS0122121	-5.86
LTS0014367	-5.86
LTS0199679	-5.85
LTS0197689	-5.82
LTS0221941	-5.82
LTS0192980	-5.80
LTS0068602	-5.79
LTS0060501	-5.79
LTS0028673	-5.79
LTS0160186	-5.78
LTS0196384	-5.78
LTS0175359	-5.78

Lotus ID	Binding free energy (kcal/mol)
LTS0185122	-5.76
LTS0071350	-5.75
LTS0253188	-5.69
LTS0028567	-5.69
LTS0082163	-5.68
LTS0029858	-5.67
LTS0218598	-5.66
LTS0042667	-5.64
LTS0025493	-5.62
LTS0037149	-5.61
LTS0110864	-5.59
LTS0198667	-5.58
LTS0120323	-5.58
LTS0118747	-5.57
LTS0181793	-5.57
LTS0018499	-5.56
LTS0184096	-5.56
LTS0210639	-5.55
LTS0122347	-5.53
LTS0127385	-5.53
LTS0017714	-5.53
LTS0052930	-5.52
LTS0079868	-5.52
LTS0224498	-5.50
LTS0197809	-5.48
LTS0012918	-5.47
LTS0171236	-5.46
LTS0012383	-5.43
LTS0056916	-5.42
LTS0210058	-5.41
LTS0076944	-5.40
LTS0260361	-5.40
LTS0092544	-5.39
LTS0051254	-5.38

Lotus ID	Binding free energy (kcal/mol)
LTS0161751	-5.38
LTS0138350	-5.36
LTS0022487	-5.36
LTS0234857	-5.35
LTS0202421	-5.34
LTS0020436	-5.33
LTS0221786	-5.33
LTS0271385	-5.31
LTS0175254	-5.27
LTS0041256	-5.27
LTS0243979	-5.26
LTS0085212	-5.23
LTS0056969	-5.23
LTS0221261	-5.22
LTS0179347	-5.20
LTS0102324	-5.20
LTS0109015	-5.20
LTS0031433	-5.20
LTS0175223	-5.19
LTS0241460	-5.18
LTS0183420	-5.17
LTS0028543	-5.16
LTS0272557	-5.15
LTS0266184	-5.14
LTS0099153	-5.13
LTS0155301	-5.11
LTS0184419	-5.08
LTS0168502	-5.01
LTS0023308	-5.00
LTS0155981	-4.88
LTS0177188	-4.87
LTS0264910	-4.85
LTS0225699	-4.81
LTS0256716	-4.80

Lotus ID	Binding free energy (kcal/mol)
LTS0115731	-4.76
LTS0227195	-4.76
LTS0047269	-4.74
LTS0028673	-4.74
LTS0024564	-4.73
LTS0228888	-4.63

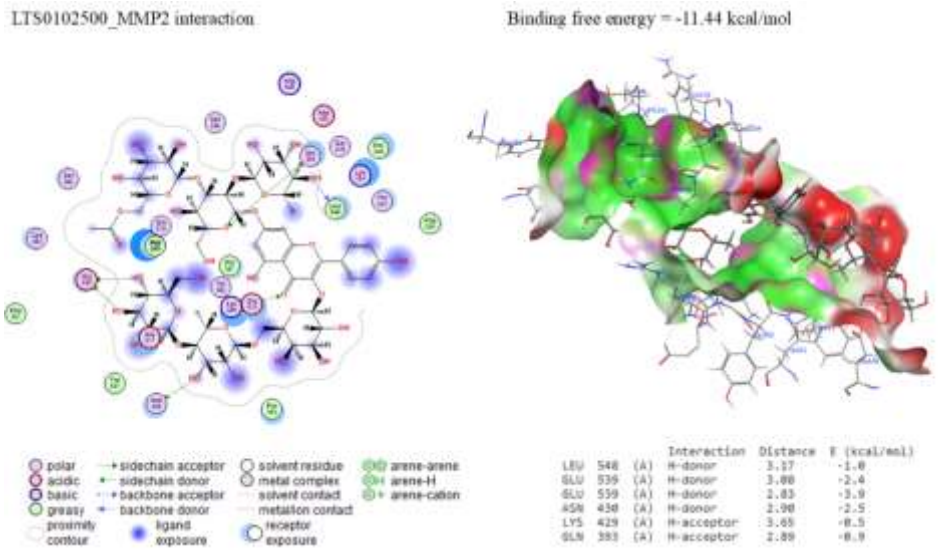

Figure 1. Molecular docking interaction of [(2r,3s,4s,5r,6s)-6-{[(2s,3r,4s,5r,6r)-2-[(3-{[(2s,3r,4s,5r,6r)-6-({[(2r,3r,4s,5r,6s)-3,4-dihydroxy-6-methyl-5-{[(2s,3r,4s,5s,6r)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy}oxan-2-yl]oxy}methyl)-3,4,5-trihydroxy-oxan-2-yl]oxy}-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-7-yl)oxy]-5-hydroxy-6-(hydroxymethyl)-3-{[(2s,3r,4r,5r,6s)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxy}oxan-4-yl]oxy}-3,4,5-trihydroxyoxan-2-yl]methyl acetate (LTS0102500) against matrix metallopeptidase 2 (MMP2).

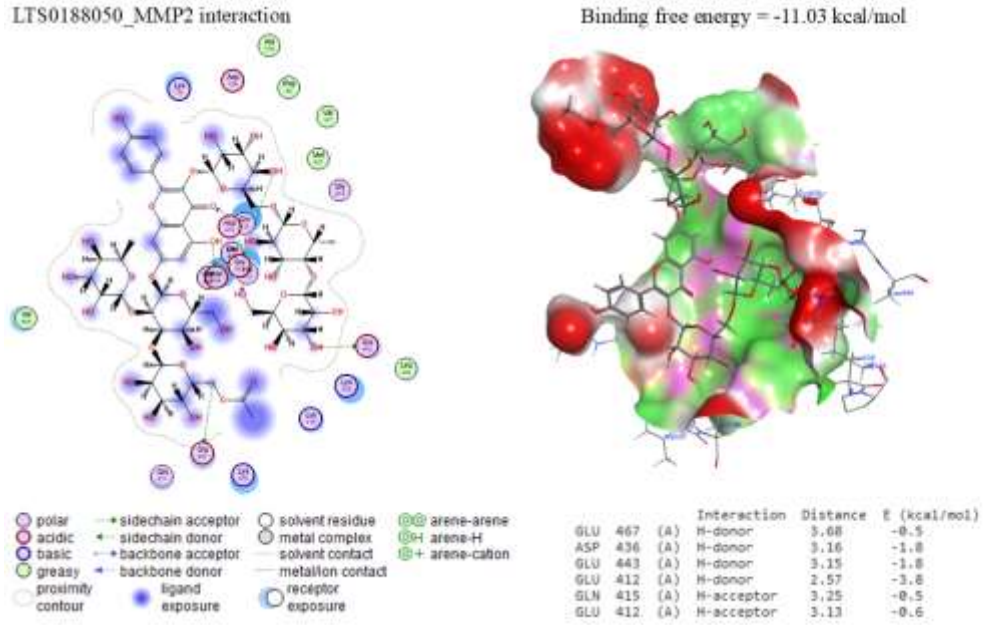

Figure 2. Molecular docking interaction of (6-{[2-({3-[(6-{[(3,4-dihydroxy-6-methyl-5-{[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy}oxan-2-yl)oxy]methyl}-3,4,5-trihydroxyoxan-2-yl)oxy]-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-7-yl}oxy)-5-hydroxy-6-(hydroxymethyl)-3-[(3,4,5-trihydroxy-6-methyloxan-2-yl)oxy]oxan-4-yl]oxy}-3,4,5-trihydroxyoxan-2-yl)methyl acetate (LTS0188050) against matrix metallopeptidase 2 (MMP2).

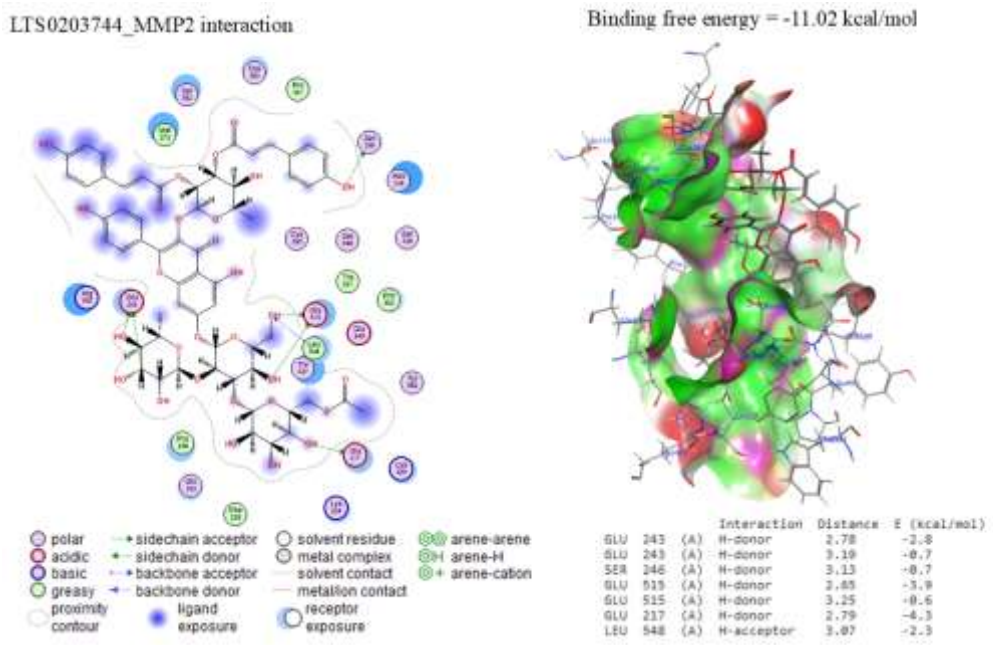

Figure 3. Molecular docking interaction of (2s,3r,4r,5s,6s)-2-[(7-{[(2s,3r,4s,5r,6r)-4-{[(2s,3r,4s,5s,6r)-6-[(acetyloxy)methyl]-3,4,5-trihydroxyoxan-2-yl]oxy}-5-hydroxy-6-(hydroxymethyl)-3-{[(2s,3r,4r,5r,6s)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxy}oxan-2-yl]oxy}-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-3-yl)oxy]-5-hydroxy-3-{[(2e)-3-(4-hydroxyphenyl)prop-2-enoyl]oxy}-6-methyloxan-4-yl (2e)-3-(4-hydroxyphenyl)prop-2-enoate (LTS0203744) against matrix metallopeptidase 2 (MMP2).

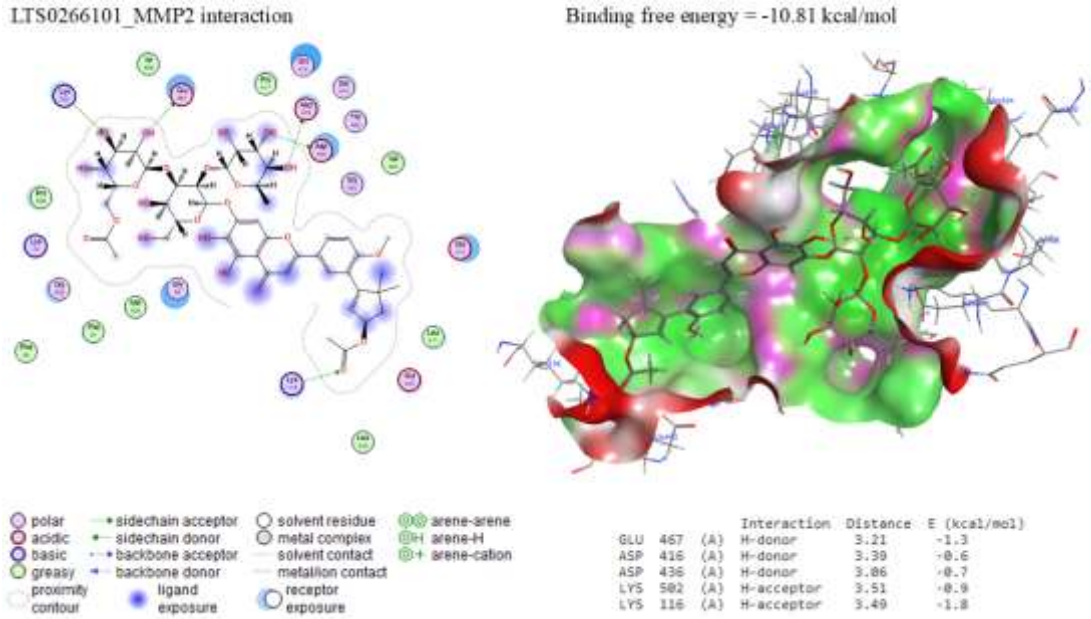

Figure 4. Molecular docking interaction of [6-({2-[(2-{3-[3-(acetyloxy)-5,5-dimethylcyclopent-1-en-1-yl]-4-methoxyphenyl}-5,6-dihydroxy-4-oxochromen-7-yl)oxy]-5-hydroxy-6-(hydroxymethyl)-3-[(3,4,5-trihydroxy-6-methyloxan-2-yl)oxy] oxan-4-yl}oxy)-3,4,5-trihydroxyoxan-2-yl]methyl acetate (LTS0266101) against matrix metallopeptidase 2 (MMP2).

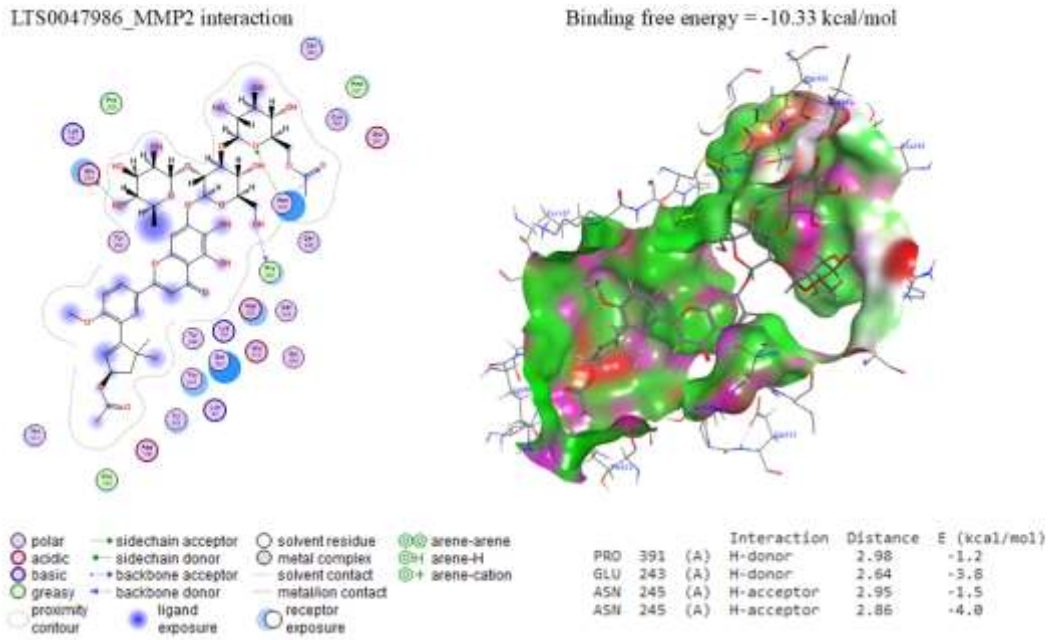

Figure 5. Molecular docking interaction of [(2r,3s,4s,5r,6s)-6-{[(2s,3r,4s,5r,6r)-2-[(2-{3-[(3r)-3-(acetyloxy)-5,5-dimethylcyclopent-1-en-1-yl]-4-methoxyphenyl}-5,6-dihydroxy-4-oxochromen-7-yl)oxy]-5-hydroxy-6-(hydroxymethyl)-3-{[(2s,3r,4r,5r,6s)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxy}oxan-4-yl]oxy}-3,4,5-trihydroxyoxan-2-yl]methyl acetate (LTS0047986) against matrix metallopeptidase 2 (MMP2).

Table 2 revealed the molecular docking interactions of COS bioactive compounds against MMP9. Among them, the [(2r,3s,4s,5r,6s)-6-[(7-{[(2s,3r,4s,5r,6r)-4-{[(2s,3r,4s,5s,6r)-6-[(acetyloxy)methyl]-3,4,5-trihydroxyoxan-2-yl]oxy}-5-hydroxy-6-(hydroxymethyl)-3-{[(2s,3r,4r,5r,6s)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxy}oxan-2-yl]oxy}-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-3-yl)oxy]-3,4-dihydroxy-5-{[(2s,3r,4s,5s,6r)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy}oxan-2-yl]methyl(2e)-3-(3,4-dihydroxyphenyl)prop-2-enoate (LTS0119846), (6-{[2-({3-[(6-{[(3,4-dihydroxy-6-methyl-5-{[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy}oxan-2-yl)oxy]methyl}-3,4,5-trihydroxyoxan-2-yl)oxy]-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-7-yl}oxy)-5-hydroxy-6-(hydroxymethyl)-3-[(3,4,5-trihydroxy-6-methyloxan-2-yl)oxy]oxan-4-yl]oxy}-3,4,5-trihydroxyoxan-2-yl)methylacetate (LTS0188050),[(2r,3s,4s,5r,6s)-6-{[(2s,3r,4s,5r,6r)-2-[(3-{[(2s,3r,4s,5r,6r)-6-({[(2r,3r,4s,5r,6s)-3,4-dihydroxy-6-methyl-5-{[(2s,3r,4s,5s,6r)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy}oxan-2-yl]oxy}methyl)-3,4,5-trihydroxyoxan-2-yl]oxy}-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-7-yl)oxy]-5-hydroxy-6-(hydroxymethyl)-3-{[(2s,3r,4r,5r,6s)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxy}oxan-4-yl]oxy}-3,4,5-trihydroxyoxan-2-yl]methyl acetate (LTS0102500), {6-[(7-{[4-({6-[(acetyloxy)methyl]-3,4,5-trihydroxyoxan-2-yl}oxy)-5-hydroxy-6-(hydroxymethyl)-3-[(3,4,5-trihydroxy-6-methyloxan-2-yl)oxy]oxan-2-yl]oxy}-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-3-yl)oxy]-3,4-dihydroxy-5-{[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy}oxan-2-yl}methyl 3-(3,4-dihydroxyphenyl) prop-2-enoate (LTS0147418), and 2-{[2-({[2-({[2-({[2-({[3,4-dihydroxy-2,5-bis(hydroxymethyl)oxolan-2-yl]oxy}methyl)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-

yl]oxy}methyl)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]oxy}methyl)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]oxy}methyl)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]oxy}-6-(hydroxymethyl)oxane-3,4,5-triol (LTS0253995) exhibited highest binding free energies of -11.69, -11.46, -11.18, -11.07, and -10.35 kcal/mol, respectively.

Table 2. Molecular docking interactions of *Saussurea costus* (COS) bioactive compounds against matrix metallopeptidase 9 (MMP9)

Lotus ID	Binding free energy (kcal/mol)
LTS0119846	-11.69
LTS0188050	-11.46
LTS0102500	-11.18
LTS0147418	-11.07
LTS0253995	-10.35
LTS0051532	-10.33
LTS0245327	-10.13
LTS0016691	-9.73
LTS0111748	-9.62
LTS0266101	-9.49
LTS0047986	-9.47
LTS0203744	-9.15
LTS0083004	-9.06
LTS0226059	-8.65
LTS0274607	-7.86
LTS0134711	-7.71
LTS0078269	-7.54
LTS0126727	-7.49
LTS0158828	-7.41
LTS0037686	-7.40
LTS0241329	-7.39
LTS0023878	-7.25
LTS0272676	-7.20
LTS0093930	-7.17
LTS0046227	-7.16
LTS0201798	-7.11
LTS0085784	-7.08

Lotus ID	Binding free energy (kcal/mol)
LTS0246208	-6.97
LTS0086283	-6.96
LTS0272557	-6.88
LTS0154111	-6.87
LTS0108243	-6.87
LTS0235378	-6.82
LTS0122121	-6.75
LTS0068602	-6.68
LTS0014367	-6.68
LTS0079178	-6.62
LTS0201557	-6.62
LTS0027205	-6.54
LTS0025493	-6.53
LTS0120323	-6.53
LTS0037149	-6.50
LTS0122347	-6.50
LTS0182111	-6.49
LTS0109015	-6.49
LTS0199679	-6.48
LTS0174867	-6.45
LTS0207678	-6.45
LTS0264682	-6.44
LTS0221261	-6.44
LTS0042759	-6.44
LTS0198920	-6.44
LTS0221941	-6.42
LTS0256764	-6.42
LTS0052930	-6.38
LTS0134703	-6.37
LTS0271385	-6.35
LTS0060501	-6.33
LTS0272033	-6.32
LTS0046559	-6.30
LTS0222542	-6.24

Lotus ID	Binding free energy (kcal/mol)
LTS0234857	-6.20
LTS0201707	-6.19
LTS0148187	-6.15
LTS0028567	-6.11
LTS0110864	-6.06
LTS0020436	-6.02
LTS0012383	-6.02
LTS0210058	-6.01
LTS0012918	-5.99
LTS0079868	-5.96
LTS0185122	-5.96
LTS0197809	-5.95
LTS0220970	-5.91
LTS0210132	-5.89
LTS0175254	-5.89
LTS0028543	-5.86
LTS0051254	-5.85
LTS0042667	-5.83
LTS0056916	-5.82
LTS0161751	-5.81
LTS0017714	-5.81
LTS0260361	-5.79
LTS0198667	-5.76
LTS0141044	-5.75
LTS0224498	-5.73
LTS0197689	-5.72
LTS0183420	-5.71
LTS0196384	-5.67
LTS0028673	-5.65
LTS0192980	-5.64
LTS0266184	-5.63
LTS0071350	-5.63
LTS0168502	-5.63
LTS0184419	-5.62

Lotus ID	Binding free energy (kcal/mol)
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LTS0127385	-5.58
LTS0047269	-5.57
LTS0160186	-5.57
LTS0082163	-5.57
LTS0102324	-5.56
LTS0079166	-5.54
LTS0228888	-5.50
LTS0175359	-5.48
LTS0264910	-5.47
LTS0056969	-5.47
LTS0243979	-5.47
LTS0031433	-5.46
LTS0221786	-5.45
LTS0227195	-5.45
LTS0179347	-5.43
LTS0181793	-5.42
LTS0172581	-5.40
LTS0175223	-5.40
LTS0171236	-5.39
LTS0029053	-5.39
LTS0024564	-5.38
LTS0076944	-5.37
LTS0184096	-5.37
LTS0059699	-5.36
LTS0022487	-5.36
LTS0225699	-5.35
LTS0099153	-5.34
LTS0253188	-5.34
LTS0023308	-5.33
LTS0118747	-5.32
LTS0210639	-5.31
LTS0041256	-5.30
LTS0155301	-5.28

Lotus ID	Binding free energy (kcal/mol)
LTS0092544	-5.27
LTS0018499	-5.24
LTS0202421	-5.22
LTS0241460	-5.21
LTS0218598	-5.17
LTS0116967	-5.11
LTS0029858	-5.10
LTS0138350	-5.10
LTS0256716	-5.05
LTS0135640	-5.03
LTS0115431	-5.03
LTS0177188	-4.98
LTS0155981	-4.92
LTS0085212	-4.84
LTS0115731	-4.71

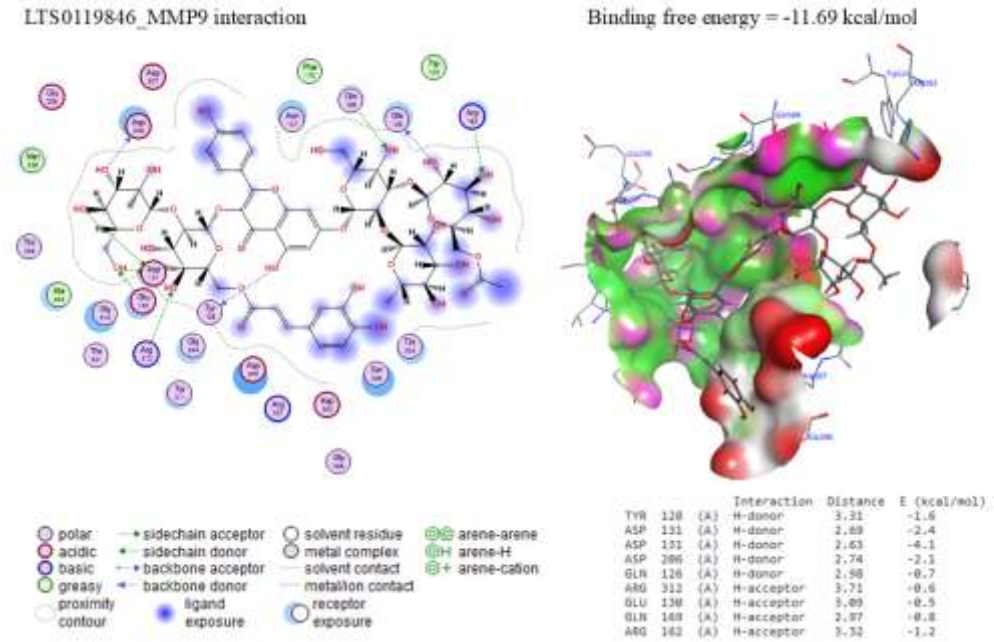

Figure 6. Molecular docking interaction of [(2r,3s,4s,5r,6s)-6-[(7-{[(2s,3r,4s,5r,6r)-4-{[(2s,3r,4s,5s,6r)-6-[(acetyloxy)methyl]-3,4,5-trihydroxyoxan-2-yl]oxy}-5-hydroxy-6-(hydroxymethyl)-3-{[(2s,3r,4r,5r,6s)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxy}oxan-2-yl]oxy}-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-3-yl)oxy]-3,4-dihydroxy-5-{[(2s,3r,4s,5s,6r)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy}oxan-2-yl]methyl (2e)-3-(3,4-dihydroxyphenyl)prop-2-enoate (LTS0119846) against matrix metallopeptidase 9 (MMP9).

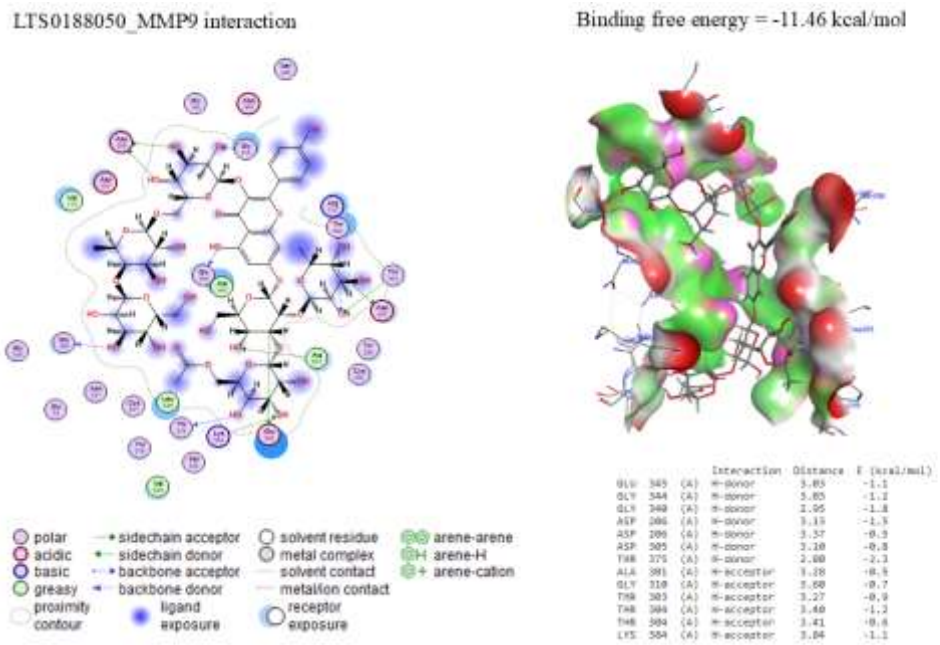

Figure 7. Molecular docking interaction of (6-{[2-({3-[(6-{[(3,4-dihydroxy-6-methyl-5-{[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy}oxan-2-yl)oxy]methyl}-3,4,5-trihydroxyoxan-2-yl)oxy]-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-7-yl}oxy)-5-hydroxy-6-(hydroxymethyl)-3-[(3,4,5-trihydroxy-6-methyloxan-2-yl)oxy]oxan-4-yl]oxy}-3,4,5-trihydroxyoxan-2-yl)methyl acetate (LTS0188050) against matrix metallopeptidase 9 (MMP9).

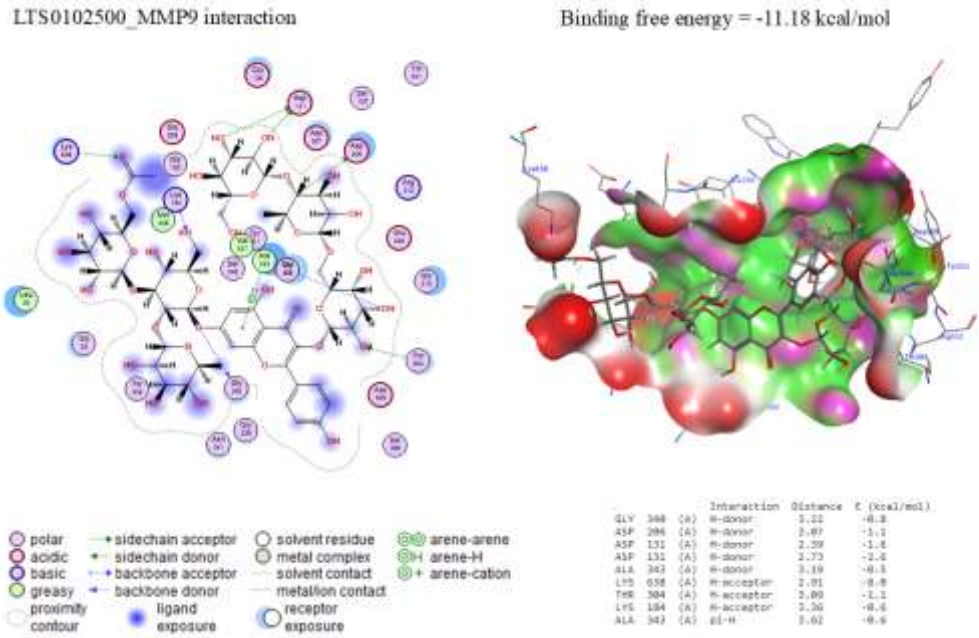

Figure 8. Molecular docking interaction of [(2r,3s,4s,5r,6s)-6-{[(2s,3r,4s,5r,6r)-2-[(3-{[(2s,3r,4s,5r,6r)-6-({[(2r,3r,4s,5r,6s)-3,4-dihydroxy-6-methyl-5-{[(2s,3r,4s,5s,6r)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy}oxan-2-yl]oxy}methyl)-3,4,5-trihydroxyoxan-2-yl]oxy}-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-7-yl)oxy]-5-hydroxy-6-(hydroxymethyl)-3-{[(2s,3r,4r,5r,6s)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxy}oxan-4-yl]oxy}-3,4,5-trihydroxyoxan-2-yl]methyl acetate (LTS0102500) against matrix metallopeptidase 9 (MMP9).

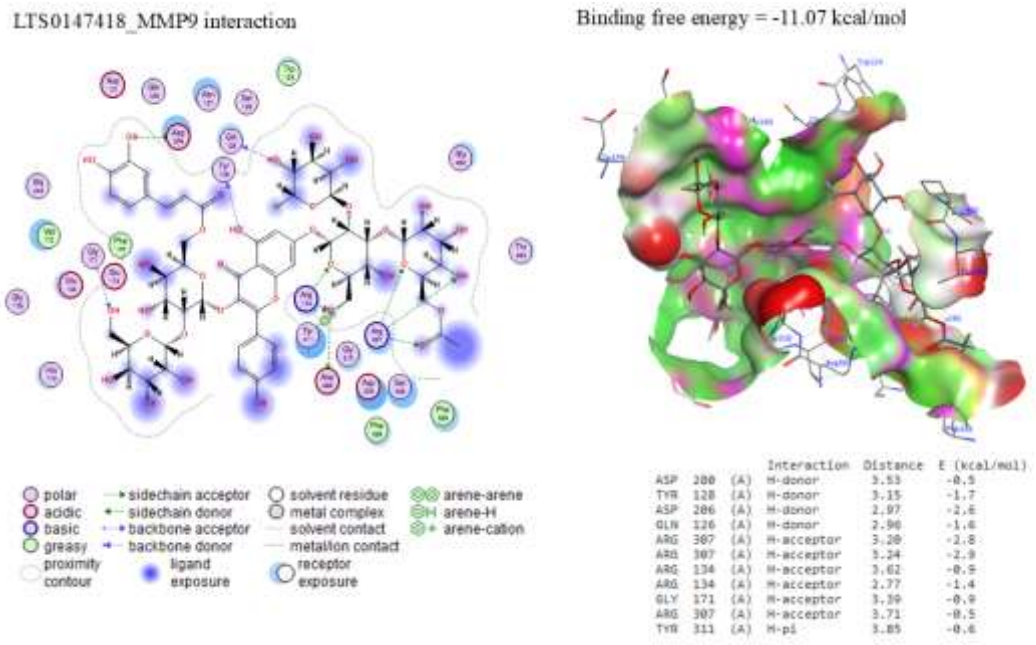

Figure 9. Molecular docking interaction of {6-[(7-{[4-({6-[(acetyloxy)methyl]-3,4,5-trihydroxyoxan-2-yl}oxy)-5-hydroxy-6-(hydroxymethyl)-3-[(3,4,5-trihydroxy-6-methyloxan-2-yl)oxy]oxan-2-yl]oxy}-5-hydroxy-2-(4-hydroxyphenyl)-4-oxochromen-3-yl)oxy]-3,4-dihydroxy-5-{[3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy}oxan-2-yl}methyl 3-(3,4-dihydroxyphenyl)prop-2-enoate (LTS0147418) against matrix metallopeptidase 9 (MMP9).

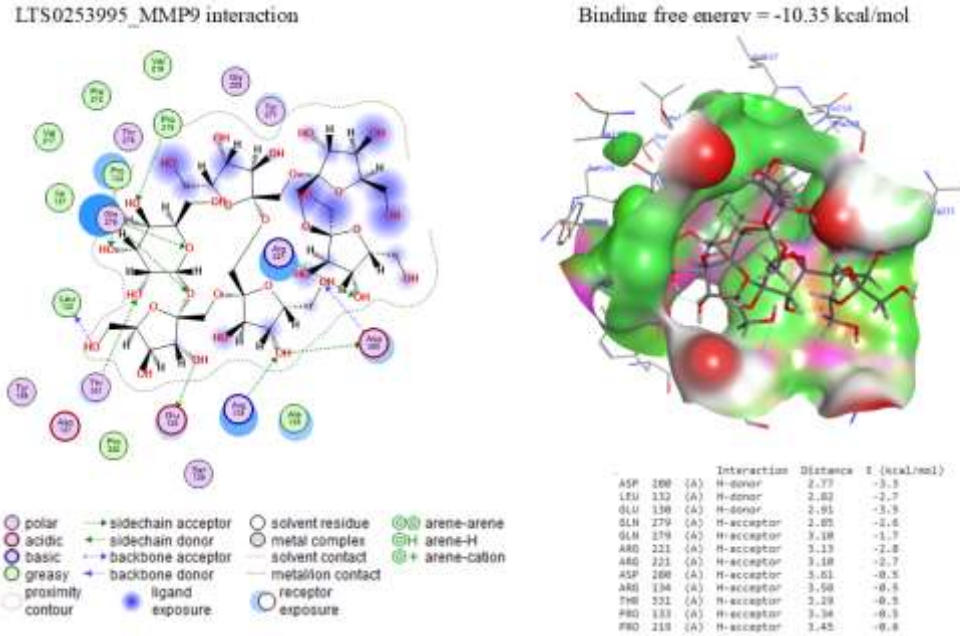

Figure 10. Molecular docking interaction of 2-{[2-({[2-({[2-({[2-({[3,4-dihydroxy-2,5-bis(hydroxymethyl)oxolan-2-yl]oxy}methyl)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]oxy}methyl)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]oxy}methyl)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]oxy}methyl)-3,4-dihydroxy-5-(hydroxymethyl) oxolan-2-yl]oxy}-6-(hydroxymethyl)oxane-3,4,5-triol (LTS0253995) against matrix metallopeptidase 9 (MMP9).

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