IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
**Research Article**
March 2023 Vol.:26, Issue: 4


# Evaluating in Silico Docking, Drug-Likeness, and QSAR Studies of Ayush Kwath as A Potential Immunomodulator

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

**Sunitha P.G*[1], Banu Priya S[2], Deattu N[3], Manimegalai P[4], Vaitheeswaran A.P.[5], Ariarasudhan V[6], Kalaiselvi G[7], Anish Mahadevan [8]**

*[1]Faculty, College of Pharmacy, Madras Medical College. Chennai, Tamil Nadu, India [2]PG Research student at College of Pharmacy, Madras Medical College. Chennai, Tamil Nadu, India [3]Faculty, College of Pharmacy, Madras Medical College. Chennai, Tamil Nadu, India [4]PG Research student at C.L. Baid Metha College of Pharmacy. India. [5]Faculty at Sri Ramachandra Medical college and Research institute. India. [6]Aeon Formulations Pvt Ltd, India. [7]PG Research student at College of Pharmacy, Madras Medical College. Chennai, Tamil Nadu, India [8] Research Student, PSG Institute of Medical Sciences & Research, India.*

**Submitted:** 22 February 2023
**Accepted:** 28 February 2023
**Published:** 30 March 2023

**Keywords:** SARS CoV2**,** Ayush Kwath, Docking, QSAR, Immunostimulatory

**ABSTRACT**

With the alarming increase in the number of Covid-19 active cases, immunostimulation has become a need for research. A wide range of ayurvedic formulations such as Nilavembu Kudineer, Kabasura Kudineer, and Sudarshan churn is prescribed as a prophylactic measure. **Objective:** This study aims to explore the drug-likeness, docking, and immunomodulatory properties of Ayush Kwath recommended by the Ministry of AYUSH. Ayush Kwath constitutes the herbs found in every Indian kitchen including cinnamon, pepper, ginger, and tulsi. **Method:** The drug-likeness of 22 compounds was evaluated and molecular docking for these compounds was performed against proteins 4QBZ, 4O9H, 2B90, and 2AZ5 by *In silico* techniques. The $EC_{50}$ of constituents was collected and selected as the training set. The chemical descriptors were calculated using Padel software. **Results:** All 22 compounds were docked with proteins and the binding energies obtained were in the range of -2.17 to -9.85. The developed QSAR model showed a high activity-descriptor relationship with an accuracy of 95% ($r^2$=0.95) and a prediction accuracy of 90%.

## INTRODUCTION

It has been almost a year, since the first SARS CoV2(Severe Acute Respiratory Syndrome Corona Virus 2) case was reported in India. Despite the usage of masks, and hand sanitizers and maintaining social distancing the cases continue to increase exponentially. India, from ranking second in the total number of active cases, the present day the active cases began declining after taking necessary precautions and preventive measures. Having hundreds of vaccines in the pre-clinical and clinical stages we are forced to look for alternatives. Ministry of AYUSH (Ayurveda, Yoga & Naturopathy, Unani, Siddha, and Homoeopathy) recommended certain steps to be taken to improve the immunity of an individual such as[1]

- Drinking hot water
- Practising yogasanas, meditation and pranayama.
- Consuming chyawanaprash (10 gm), Golden milk (150ml) and Ayush Kadha.

Immunomodulators are medications that help to regulate or normalize the immune system. These include Immunoadjuvants, Immunostimulants, and Immunosuppressants. Immunoadjuvants enhance the efficacy of vaccines and therefore could be considered specific immune stimulants. Immunostimulants act by innate as well as adaptive immune responses. Immunosuppressants are often used to treat graft rejections and autoimmune diseases. [2] The phytochemical analysis of rasayana plants has revealed that a large number of compounds possess potent immunomodulatory properties[3]. Especially ursolic acid showed antimicrobial activity plus an immune-stimulatory effect.[4] Moreover, ginger and tulsi were tested for their immunostimulant activities against cancer and the constituents rosmarinic-acid and luteolin was found to be active phytochemicals.[5] This study focuses on the immunostimulatory potential of all the major active constituents identified from the constituents of Ayush kwath.

### Phytoconstituents:

Ayush Kwath or Ayush Kudineer or Ayush Joshanda is a combination of four medicinal herbs commonly used in every Indian kitchen - Basil leaves (tulsi), Cinnamon bark (dalchini), *Zingiber officinale* (sunthi), and Krishna marich (*Piper nigrum*).

**Preparation procedure:**

Four parts of Tulsi (*Ocimum sanctum*) leaves, 2 parts of Dalchini (*Cinnamomum zeylanicum*) stem bark, 2 parts of Sunthi (*Zingiber officinale*) rhizome, and 1 part of Krishna marich (*Piper nigrum*) fruit are powdered. Three grams of powder- comprising all ingredients are dissolved in 150ml boiled water. Jaggery, raisin, or lemon juice can be added to the decoction.[6]A list of major active constituents is furnished in Table 1.

**Table No 1. Major phytoconstituents identified**

| S.No | Constituents |
|---|---|
| 1 | Alpha-Cubebene |
| 2 | Apigenin |
| 3 | Beta bisabolene |
| 4 | Carvacrol |
| 5 | Caryophyllene |
| 6 | Cinnamaldehyde |
| 7 | Cirsilineol |
| 8 | Cirsimaritin |
| 9 | Dipiperamide D |
| 10 | Dipiperamide E |
| 11 | Eugenol |
| 12 | Gingerol |
| 13 | Isothymusin |
| 14 | Linalool |
| 15 | Piperine |
| 16 | Piperitone |
| 17 | Rosmarinic acid |
| 18 | Shogaol |
| 19 | Ursolic acid |
| 20 | Wisanine |
| 21 | Zerumbone |
| 22 | Zingiberene |

## MATERIALS AND METHODS

### Drug-likeness:

One of the most traditional methods to evaluate the drug-likeness of a compound is by using Lipinski's rule of five. This was estimated using the online software SwissADME. [7] Ghose, Veber, Egan, and Mueggeare other filters used to evaluate drug-likeness.

### QSAR:

Quantitative Structure-Activity Relationship (QSAR) models are theoretical models that relate a quantitative measure of chemical structure to a physical property, or a biological activity. A total of 22 major phytoconstituents with immunomodulatory were collected from various databases and literature.22 phytoconstituents were selected based on their availability in plants. The effective dose $EC_{50}$ of constituents was collected from various articles.[8-18]Nine compounds were selected as the training set. Four compounds were taken as a test set. The compounds were downloaded and energy was minimized. Molecular descriptors were calculated by using Padel Descriptor. The descriptors include 2D descriptors such as AlogP, autocorrelation, atom count, atom type electron topological state descriptors, Crippen's logP and molar refractivity ring count, molecular linear free energy relation descriptors, etc. The QSAR model development was done by using DTC based on the MLR method. For validation of the developed QSAR model LOO method was used and external validation ($r^2$) is carried out to predict the accuracy of the QSAR model. Correlation coefficient (r) quantifies the variation in the data and gives an idea of how closely the observed data tracks the fitted regression line. A perfect relation has r = +1 (positively correlated) or -1 (negatively correlated); no correlation has r = 0. The more scattered the data points, the lower the value of r.Leave-one-out (LOO) method was used for internal cross-validation regression coefficient ($r^2_{cv}$), each molecule in the training set was eliminated once and the activity of the eliminated molecule was predicted by using the model developed by the remaining molecules. [19] The cross-validation regression coefficient was calculated using the equation which describes the internal stability of a model.

$$r^2 = 1 - \frac{\sum(Ypred-Y)2}{\sum(Y-\ddot{Y})2}$$

where $r^2_{cv}$ refers to cross-validation regression coefficient, Y and Ypred activity of the molecule in the training set, respectively and Ÿ is the average activity of all molecules in the

training set. The activity of each molecule in the test set was predicted using the model developed by the training set for external validation.

**Molecular docking:**

The proteins were downloaded from Protein Data Bank (RCSB PDB) and processed with Molegro Molecular Viewer 2.5.0. Crystal structure of human TLR8 (Toll-Like Receptor 8) in complex with DS-802 (4QBZ), Crystal structure of the interleukin-4 (2B90), Structure of Interleukin-6 in complex with a Camelid Fab fragment (4O9H), Crystal Structure of TNF-alpha with a small molecule inhibitor (2AZ5) were obtained. All the proteins were recovered by X-ray diffraction with resolutions 2.00 Å, 2.10 Å, 2.42 Å, and 2.10 Å respectively. Ligands were downloaded from PubChem and energy was minimized in Chem 3D Ultra 8.0. The protein-ligand complexes were analyzed in Molegro Molecular Viewer 2.5.0. and Pymol.

**RESULTS AND DISCUSSION**

**Drug-likeness:**

Major active constituents were estimated for their drug-likeness according to Lipinski's rule of five and the violations were tabulated. Seven constituents violate one factor of Lipinski's rule of five. There is a permissible limit of not more than two violations and hence all the active constituents are found to possess drug-likeness [20], the results of which are given in Table 2.

**Table no 2. Drug-likeness of the phytoconstituents**

| S.No. | Constituent | Molecular formula | Molecular weight (g/mol) | Druglikeness |
|---|---|---|---|---|
| 1 | Alpha-Cubebene | $C_{15}H_{24}$ | 204.35 | Yes; 1 violation: MLOGP>4.15 |
| 2 | Apigenin | $C_{15}H_{10}O_5$ | 270.24 | Yes |
| 3 | Beta bisabolene | $C_{15}H_{24}$ | 204.35 | Yes; 1 violation: MLOGP>4.15 |
| 4 | Carvacrol | $C_{10}H_{14}O$ | 150.22 | Yes |
| 5 | Caryophyllene | $C_{15}H_{24}$ | 204.35 | Yes; 1 violation: MLOGP>4.15 |
| 6 | Cinnamaldehyde | $C_9H_8O$ | 132.16 | Yes |
| 7 | Cirsilineol | $C_{18}H_{16}O_7$ | 344.32 | Yes |
| 8 | Cirsimaritin | $C_{17}H_{14}O_6$ | 314.29 | Yes |
| 9 | Dipiperamide D | $C_{36}H_{40}N_2O_6$ | 596.71 | Yes; 1 violation: MW>500 |
| 10 | Dipiperamide E | $C_{34}H_{38}N_2O_6$ | 570.68 | Yes; 1 violation: MW>500 |
| 11 | Eugenol | $C_{10}H_{12}O_2$ | 164.2 | Yes |
| 12 | Gingerol | $C_{17}H_{26}O_4$ | 294.39 | Yes |
| 13 | Isothymusin | $C_{17}H_{14}O_7$ | 330.29 | Yes |
| 14 | Linalool | $C_{10}H_{18}O$ | 154.25 | Yes |
| 15 | Piperine | $C_{17}H_{19}NO_3$ | 285.34 | Yes |
| 16 | Piperitone | $C_{10}H_{16}O$ | 152.23 | Yes |
| 17 | Rosmarinic acid | $C_{18}H_{16}O_8$ | 360.31 | Yes |
| 18 | Shogaol | $C_{17}H_{24}O_3$ | 276.37 | Yes |
| 19 | Ursolic acid | $C_{30}H_{48}O_3$ | 456.7 | Yes; 1 violation: MLOGP>4.15 |
| 20 | Wisanine | $C_{18}H_{21}NO_4$ | 315.36 | Yes |
| 21 | Zerumbone | $C_{15}H_{22}O$ | 218.33 | Yes |
| 22 | Zingiberene | $C_{15}H_{24}$ | 204.35 | Yes; 1 violation: MLOGP>4.15 |

MW-Molecular weight

MLOGP- Moriguchi logP calculated using SwissADME [21]

**QSAR:**

In the present work, the structural activity relationship is represented by developing a QSAR model that relates the 2D chemical descriptors with the biological activity. A set of 13 constituents were used for developing the QSAR model. The descriptor values and pEC50 values are given in Table 3.

**Table 3. Values of molecular descriptors and pEC50 values for training and test set.**

| Compound number | Compound name | MR | nC | GATS8s | SpMax_DzZ | CrippenMR | Observed pEC50 |
|---|---|---|---|---|---|---|---|
| 1 | Apigenin | 69.85 | 15 | 1.058035 | 60.75699 | 74.8344 | -1.19 |
| 2 | Caryophyllene | 66.59 | 15 | 0 | 43.58518 | 66.203 | -0.256 |
| 3 | Cinnamaldehyde | 42.82 | 9 | 4.708587 | 19.82403 | 43.721 | 1.31 |
| 4 | Gingerol | 82.94 | 17 | 0.908696 | 102.959 | 85.9956 | 0.127 |
| 5 | Piperine | 82.14 | 17 | 1.336948 | 86.91907 | 85.142 | 0.795 |
| 6 | Ursolic acid | 133.52 | 30 | 1.080307 | 157.4421 | 135.5846 | 1.207 |
| 7 | Rosmarinic acid | 91.35 | 18 | 0.806936 | 119.5087 | 91.978 | 2.508 |
| 8 | Shogaol | 81.51 | 17 | 0.851925 | 93.50669 | 84.2418 | -0.447 |
| 9 | Zerumbone | 68.4 | 15 | 0.879679 | 46.14586 | 71.726 | 0.414 |
| $10^T$ | Carvacrol | 47.14 | 10 | 0 | 22.91476 | 48.521 | -2.426 |
| $11^T$ | Eugenol | 48.72 | 10 | 2.187413 | 26.80388 | 50.709 | 0.884 |
| $12^T$ | Linalool | 49.5 | 10 | 0.345941 | 30.074 | 48.9458 | 1.602 |
| $13^T$ | Piperitone | 45.97 | 10 | 0 | 25.46987 | 49.299 | -1.557 |

MR-Molar Refractivity

nC- Number of Carbon atoms

GATS8s and SpMax_DzZ are autocorrelations and Burden modified eigenvalues respectively

CrippenMR- Crippen Molar Refractivity

pEC50- negative log of Effective concentration 50

The developed QSAR model showed a high activity-descriptor relationship with an accuracy of 95% ($r^2$=0.95) and a prediction accuracy of 90%. The model is developed using five descriptors such as molar refractivity, number of the carbon atom, autocorrelation (GATS8s), Burden modified eigenvalues (SpMax_DzZ) and Crippen MR correlated with immunostimulatory activity. The QSAR mathematical model equation derived through MLR (developed using DTC laboratory) is given below, representing the relationship between *in vivo* effective concentration ($EC_{50}$) and chemical descriptors:

**Predicted log $EC_{50}$(mg)= -13.5108(+/-3.65872)+1.34982(+/-0.28727)*molar refractivity -2.83894(+/-0.79643)*nC +0.99685(+/-0.33596)*GATS8s-0.16204(+/-0.0537) *SpMax_DzZ -0.41123(+/-0.13294)*CrippenMR**

**$r^2$=0.95, $q^2$=0.94**

The values predicted using the developed QSAR model are given in Table 4.

**Table No 4. Comparison of experimental and predicted activity data calculated through the QSAR model based on best correlated chemical descriptors.**

| Compound number | Compound name | Predicted activity | Observed pEC50 |
|---|---|---|---|
| 1 | **Alpha-Cubebene** | **-1.86497** | |
| 2 | **Beta-bisabolene** | **0.047491** | |
| 3 | **Cirsilineol** | **2.661634** | |
| 4 | **Cirsimaritin** | **1.176674** | |
| 5 | **Dipiperamide D** | **5.239269** | |
| 6 | **Dipiperamide E** | **1.841495** | |
| 7 | **Isothymusin** | **2.485849** | |
| 8 | **Wisanine** | **2.710736** | |
| 9 | **Zingiberene** | **0.377995** | |
| 10 | Apigenin | -1.37408 | -1.19 |
| 11 | Caryophyllene | -0.49723 | -0.256 |
| 12 | Cinnamaldehyde | 2.31004 | 1.31 |
| 13 | Gingerol | -0.69377 | 0.127 |
| 14 | Piperine | 0.136707 | 0.795 |
| 15 | Ursolic acid | -1.93585 | 1.207 |
| 16 | Rosmarinic acid | 0.847432 | 2.508 |
| 17 | Shogaol | 1.337369 | -0.447 |
| 18 | Zerumbone | 1.358373 | 0.414 |
| 19 | Carvacrol | 1.565397 | -2.426 |
| 20 | Eugenol | -0.95978 | 0.884 |
| 21 | Linalool | 0.259828 | 1.602 |
| 22 | Piperitone | -4.2491 | -1.557 |

The validation is carried out by Leaving one out validation and external validation. Here, the external validation is 0.90, which indicates a prediction accuracy of 90% and $q^2$ value of 0.94. A prediction accuracy value of 70% and above is favorable. $r^2$ indicates the correlation between the activity (dependent variable) and descriptors (independent variable) for the training set compounds. From the model, descriptors such as molar refractivity, and GATS8s showed a positive correlation with the activity, where an increase in the value of the descriptor increases the activity. Descriptors such as a number of carbon atoms, SpMax_DzZ and CrippenMR showed negative correlation, where activity increases with the decreased

value of descriptors. Thus, the developed QSAR model holds good for the prediction of immunostimulatory activity. Figure 1 indicates the scatter plot of observed and predicted activity.

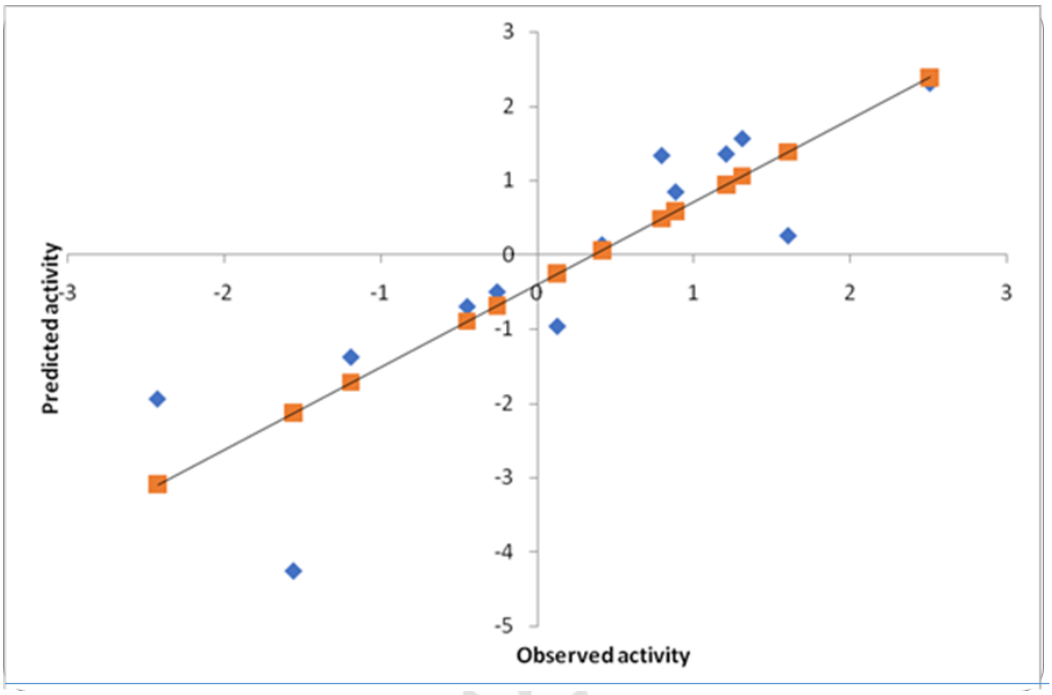


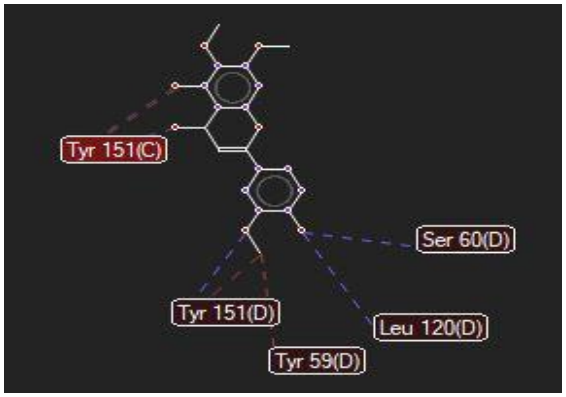

**Figure no 1. Scatter plot depicting the predicted and observed activity**

**Molecular docking:**

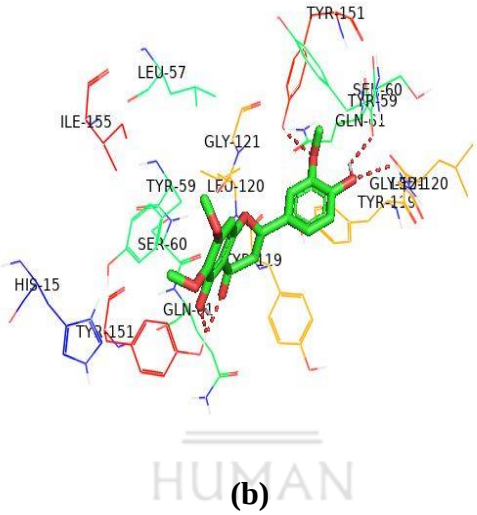
The docking results obtained for TLR8 (4QBZ) ranged from -2.17 to -8.43. The best binding energy was observed with Dipiperamide E and Piperine. The docking results obtained for interleukin-4 (2B90) ranged from-2.55 from -6.84 and IL6 (4O9H) binding energies ranged from -0.9 to -6.21. Crystal Structure of TNF-α (2AZ5) possessed a good binding energy with curvilineal (-8.13), Dipiperamide D (-9.79), Dipiperamide E (-9.85), Wisanine (-8.02), and ursolic acid (-8.89). The binding energy of all the ligands against four receptors is given in Table 5. Figure 2 depicts the binding of cirsilineol with TNF-alpha.

**Table no 5. Binding energies in Kcal/mol of the selected phytoconstituents against selected immunomodulatory receptors**

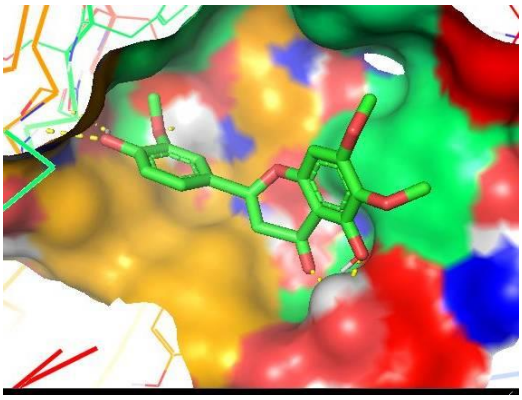
| S.No. | Constituent | Binding energy (kcal/mol) | | | |
|---|---|---|---|---|---|
| | | 4QBZ | 2B90 | 4O9H | 2AZ5 |
| 1 | Alpha-Cubebene | -5.66 | -5.08 | -4.76 | -5.41 |
| 2 | Apigenin | -7.04 | -3.69 | -5.56 | -5.64 |
| 3 | Beta bisabolene | -4.38 | -3.47 | -3.53 | -5.93 |
| 4 | Carvacrol | -5.67 | -5.43 | -3.46 | -4.8 |
| 5 | Caryophyllene | -6.4 | -4.64 | -4.84 | -6.24 |
| 6 | Cinnamaldehyde | -5.04 | -3.85 | -4.31 | -4.81 |
| 7 | Cirsilineol | -5.22 | -4.84 | -4.91 | -8.13 |
| 8 | Cirsimaritin | -6.63 | -5.22 | -5.32 | -6.67 |
| 9 | Dipiperamide D | -6.11 | -5.32 | -6.4 | -9.79 |
| 10 | Dipiperamide E | -7.2 | -6.84 | -6.07 | -9.85 |
| 11 | Eugenol | -4.77 | 3.76 | -3.69 | -3.95 |
| 12 | Gingerol | -5.08 | -2.85 | -0.9 | -4.57 |
| 13 | Isothymusin | -6.36 | -6.82 | -5.23 | -6.93 |
| 14 | Linalool | -4.15 | -3.82 | -3.42 | -4.85 |
| 15 | Piperine | -8.43 | -5.64 | -5.81 | -7.43 |
| 16 | Piperitone | -4.7 | -5.14 | -4.21 | -5.08 |
| 17 | Rosmarinic acid | -5.25 | -2.69 | -5.73 | -5.58 |
| 18 | Shogaol | -2.17 | -2.55 | -1.85 | -3.26 |
| 19 | Ursolic acid | -6.6 | -6.09 | -6.21 | -8.89 |
| 20 | Wisanine | -5.88 | -5.1 | -5.52 | -8.02 |
| 21 | Zerumbone | -6.54 | -4.58 | -5.21 | -5.15 |
| 22 | Zingiberene | -4.77 | -3.73 | -4.16 | -5.11 |




**(a)**




**(b)**



**(c)**

**Figure 2. Cirsilineol binding with TNF-alpha (2AZ5) (a) shows the 3D amino acids interaction with cirsilineol. (b) shows the 2D amino acids' interaction with cirsilineol. (c) the mesh surfaces binding pocket of cirsilineol in TNF-alpha (2AZ5).**

## CONCLUSION

The major phytoconstituents from Ayush Kwath were identified and downloaded from ligand databases. The drug-likeness of the constituents was evaluated using Lipinski's rule of five. The ligands were docked against immunomodulatory receptors like TLR 8, IL-4, IL-6, and TNF-alpha. Compounds like apigenin, cl, cirsimaritin, dipiperamide D, dipiperamide E, isothymusin, piperine, and ursolic acid provided good binding energies. The QSAR analysis established the immunostimulatory activity of the corresponding compounds. The developed QSAR model showed a high activity-descriptor relationship with an accuracy of 95% ($r^2$=0.95) and a prediction accuracy of 90%. A forward feed multiple linear regressions QSAR model was developed using a leave-one out approach for the prediction of immunomodulatory activity and no significant differences were observed in the predicted and observed activities.

**Funding:**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Acknowledgements:**

We are thankful to the College of Pharmacy, Madras Medical College, Chennai and Aeon formulations pvt ltd, Chennai for the support and encouragement rendered in carrying out this work.

## REFERENCES:

1. https://www.ayush.gov.in/ Last accessed: 04/02/2021
2. Kumar D, Arya V, Kaur R, et al. A review of immunomodulators in the Indian traditional health care system.Journal of Microbiology, Immunology and Infection,2012,Jun 1;45(3):165-84. https://doi.org/10.1016/j.jmii.2011.09.030
3. Shukla S, Bajpai VK, et al. Plants as potential sources of natural immunomodulators Reviews in Environmental Science and Bio/Technology, 2014 Mar 1;13(1):17-33. https://doi.org/10.1007/s11157-012-9303-x
4. Jiménez-Arellanes A, Luna-Herrera J, et al. Ursolic and oleanolic acids as antimicrobial and immunomodulatory compounds for tuberculosis treatment. BMC complementary and alternative medicine, 2013 Dec 1;13(1):258. https://doi.org/10.1186/1472-6882-13-258
5. Hegde PB, Samant LR. In-silico immunomodulator activity of photochemical from Zingiber officinale R., Solanum lycopersicum L, and Ocimum tenuiflorum L. against Breast cancer.IOSR Journal of Biotechnology and Biochemistrydoi: 10.9790/264X-0404014752
6. https://www.ayush.gov.in/index.htmlLast accessed: 04/02/2021
7. http://www.swissadme.ch/Last accessed: 07/02/2021

8. de Menezes Epifanio NM, Cavalcanti LR, et al .Chemical characterization and in vivo antioxidant activity of parsley (Petroselinum crispum) aqueous extract. Food & Function; 2020. doi: 10.1039/d0fo00484g
9. Chen F, Shi Z, et al. Antioxidant and antibacterial activities of eugenol and carvacrol-grafted chitosan nanoparticles. Biotechnology and bioengineering, 2009 Sep 1;104(1):30-9. doi: 10.1002/bit.22363
10. https://www.ebi.ac.uk/chembl/g/#browse/activities/filter/molecule_chembl_id%3A(%22CHEMBL445740%22)Last accessed: 04/02/2021
11. Mahboub R, Memmou F. Antioxidant activity and kinetics studies of eugenol and 6-bromoeugenol. Natural Product Research, 2015 May 19;29(10):966-71.
https://doi.org/10.1080/14786419.2014.958738
12. https://www.ebi.ac.uk/chembl/g/#browse/activities/full_state/eyJsaXN0Ijp7InNldHRpbmdzX3BhdGgiOiJFU19JTkRFWEVTX05PX01BSU5fU0VBUkNILkFDVElWSVRZIiwiY3VzdG9tX3F1ZXJ5IjoibW9sZWN1bGVfY2hlbWJsX2lkOihcIkNIRU1CTDMyNDg0MlwiKSIsInVzZV9jdXN0b21fcXVlcnkiOnRydWUsInNlYXJjaF90ZXJtIjoiIiwiYXRfbGVhc3Rfb25lX2ZhY2V0X2lzX3NLast accessed: 04/02/2021
13. Faitanin RD, Gomes JV, et al. Chemical study and evaluation of antioxidant activity and α-glucosidase inhibition of Myrciariastrigipes O. Berg (Myrtaceae). Journal of Applied Pharmaceutical Science, 2018 Mar;8(03):120-125.
https://dx.doi.org/10.7324/JAPS.2018.8317
14. Al-Tahtawy RH, El-Bastawesy AM, et al. Antioxidant activity of the volatile oils of Zingiber officinale (ginger). Spatula DD. 2011;1(1):1-8.doi: 10.5455/spatula.20101209111419
15. Nag A, Bandyopadhyay M, et al. Antioxidant activities and cytotoxicity of Zingiber zerumbet (L.) Smith rhizome. J PharmacognPhytochem, 2013 Sep;2(3):102-8.
16. Kittisakulnam S, Saetae D, Suntornsuk W. Antioxidant and antibacterial activities of spices traditionally used in fermented meat products. Journal of Food Processing and Preservation, 2017 Aug;41(4): e13004. https://doi.org/10.1111/jfpp.13004
17. da Silva JK, Andrade EH, et al. Antioxidant capacity and larvicidal and antifungal activities of essential oils and extracts from Piper krukoffii. Natural Product Communications, 2011 Sep;6(9).
https://doi.org/10.1177/1934578X1100600936
18. Chikhi I, Dergal F, et al. Chemical composition and antioxidant activity of Solenostemmaoleifolium essential oil from Southern Algeria. Journal of Applied Biotechnology Reports, 2019 Jun 17;6(2):50-4.
doi: 10.29252/JABR.06.02.02
19. Wu J, Mei J, et al. A self-adaptive genetic algorithm-artificial neural network algorithm with leave-one-out cross validation for descriptor selection in QSAR study. Journal of computational chemistry, 2010 Jul 30;31(10):1956-6. doi: 10.1002/jcc.21471
20. Bhatt JD, Chudasama CJ, et al. Pyrazole clubbed triazolo [1, 5-a] pyrimidine hybrids as an anti-tubercular agent: Synthesis, in vitro screening and molecular docking study. Bioorganic & medicinal chemistry, 2015 Dec 15;23(24):7711-6.
https://doi.org/10.1016/j.bmc.2015.11.018
21. Moriguchi I, HIRONO S, et al. Simple method of calculating octanol/water partition coefficient. Chemical and pharmaceutical bulletin. 1992 Jan 25;40(1):127-30.