Phytochemical Screening of *Adathodai Kudineer* A Siddha Herbal concoction and Evaluation of its binding affinity with SARS-CoV-2 Spike Protein and ACE2 Receptor Spike protein Complex through Molecular Docking in silico approach

**Research Article**

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**Abstract**

*Adathodai kudineer* (AK) a Classical Siddha formulation is used to treat various fevers which cause moderate to severe acute respiratory symptoms as is indicated in the text. GC-MS analysis was carried out to identify the presence of potent lead molecules in AK against novel corona virus. The aqueous extract has shown the following bioactive compounds such as Napthalene, Benzene Propanol, Benzene Acetic Acid, Furazan-3-amine, Pyrazol-4-Carboxylic acid, 2(3H) Furanone. The ethanolic extract of AK exhibited the molecular compounds such as Eucalyptol, Toluene, 2-Carene, Alpha-Copaene, 1,6-Cyclocdecadiene, Aromadendrene, Gamma-murolene, Beta-copaene, Cubebol, Selina-3,7 (11) - Diene, 2-Butanone. Molecular docking is a powerful approach in current trends to identify the possibility of pharmacological effects of medicinal compounds which could be exerted over their Corresponding Protein targets which are relevant for causing disease. Using Auto dock Vina Software, the biomolecules of AK were analyzed through molecular docking against SARS-CoV-2 Spike Protein (PDB ID 6LU7) and SARS-CoV-2 Spike Protein – ACE 2 receptor complex (6LZG). ADME properties were also recorded for the aqueous and ethanolic extracts of AK compounds using online tool SWISS ADME. The binding energy observed were of the order: -10.9 Kcal/mol, -8.0 Kcal/mol, -7.8 Kcal/mol for the compounds Alpha-Copaene, Gamma-Murolene, Selina-3,7 (11) –Diene respectively towards the protein target 6LZG and -8.2 Kcal/mol, -6.6 Kcal/Mol, -6.5 Kcal/Mol, for the compounds Alpha-Copaene, Cubebol, Aromadendrene respectively towards for the target 6LU7. These findings confirm that the Siddha formulation *Adathodai Kudineer* has some potent activity against SARS-CoV-2 Virus COVID19 disease.

**Key Words:** *Adathodai Kudineer*, ADME, Siddha medicine, Protein–Protein Interaction, Molecular Docking, COVID 19.

**Introduction**

Emerging of Viral diseases like SARS, H1N1 influenza, MERS-CoV as epidemic in past decades. Now the current scenario in the entire world is facing a pandemic situation of Corona Viral infection which first emerges in Wuhan, China. World health organization declared the global health emergency due to COVID19 outbreak. The COVID 19, a disaster of 2020 has affected almost all the countries of the world with increasing death rates. As of 24 April 2021, there have been 145,216,414 confirmed cases of COVID-19, including 3,079,390 deaths, reported to WHO (1). It was identified that the Novel Beta Corona Virus named SARS-CoV2 is the causative organism behind the outbreak of COVID19.

It is currently estimated that the incubation of SARS-CoV2 infection is between 2-14 days before the symptom’s onset such as fever, cough, Sore Throat, dyspnea and the median disease incubation period was calculated as 5.1 days by the researchers of Johns Hopkins Bloomberg School of Public Health. The rapid transmission is occurred in COVID 19 is due to its person to person transmission is highly efficient and through respiratory droplets. The SARS-CoV2 is infecting the host cells by entering into the Human ACE 2 receptors through its enveloped spike glycoprotein (2). The primary target of the COVID 19 causing virus is the lung epithelial cells. The risk factors were assessed based on the available clinical data such as Hypertension, Cardiovascular Conditions, Cancer and Diabetes Mellitus.

Research Studies are being conducted to identify the impairment in response of antibody to SarsCoV2 infection, quantification of viral load, viral shedding prolongment in immunocompromised COVID 19 affected individuals. Immunity plays a significant role while challenging with viral infections. Some traditional Siddha medicines are being unique in treating viral infections at various stages including at the time of pathogenesis, prognosis due to its potent antiviral pharmacological
Results and Ethanolic extract of Siddha drug GCMS analysis L. (Adathodai (8). The drug AK has the following 4 herbals such as prepared as per the Siddha text

Materials and Methods

Source of drug

The Sastric drug Adathodai Kudineer was prepared as per the Siddha text Siddha Vaithya Thirattu (7) (8). The drug AK has the following 4 herbs such as Adathodai (Justicia adhatoda L.), Adhimadhuram (Glycyrrhiza glabra L.), Thaalisapathiri (Taxus buccata L.), Arisi Thippilli (Piper longum L.).

GCMS analysis

GCMS analysis was carried out on the Aqueous and Ethanolic extract of Siddha drug Kabasura kudineer at the NABL accredited laboratory (Bureau veritas) in Chennai as per the standard protocol.

Protein preparation

The SARS-CoV-2 Virus main protease complex with an inhibitor N3 3D structure (PDBid: 6LU7) and Spike protein bound with ACE2 receptor protein molecule structure (PDBid: 6LZG) was retrieved from the Protein Data Bank (PDB) and energy minimized and then converted into their respective PDBQT formats. 2d. Ligand preparation:
The lead molecules were identified in the Siddha formulation achieved through GCMS analysis such as Naphthalene, Benzene Propanol, Benzene Acetic Acid, Furazan-3-amine, Pyrazol-4-Carboxylic acid, 2(3H) Furanone, Eucalyptol, Toluene, 2-Carene, Alpha-Copaene, 1,6-cyclodecadiene, Aromadendrene, Gamma-murolene, Beta-copaene, Cubebol, Selina-3,7 (11) - Diene, 2-Butanone were selected as ligands for docking. 3D structures of the above mentioned selected ligands taken from PubChem structures and were minimized by applying Gnaasstiere charge and colemann charge the root of the structure was detected torsion applied and the structures were saved in PDBQT format which is regularly used in Molecular docking analysis (9).

Molecular Docking

Molecular Docking analysis performed with a commonly well-known established software Auto dock Vina a very convenient and excellent screening tool for identifying binding energy between the 3D structures of each ligand and target proteins (10). Two target proteins PDB ID: 6LU7 and PDB ID: 6LZG were selected, a Grid-free docking performed, and the binding energies of each ligand found.

ADME properties prediction

The ADME (Adsorption, dissociation, Metabolism and excretion) properties of above mentioned natural compounds predicted using Swiss ADME an online tool for ADME prediction (11).

Protein-Ligand interaction profile

Amino acids interactions of the ligands and their relation with the natural bonds were identified using a software tool Ligplot++. (10). All the results were summarized and interpreted.

Table 1. Phytocomponents Identified In The Aqueous Extract Of Medicinal Compound AdathodaiKudineer

| S.No | RT   | Area % | Library/ID                  | Mol. F     | Mol. W (g/mol) |
|------|------|--------|----------------------------|------------|---------------|
| 1    | 12.430 | 24.69  | Naphthalene (C\Database\NIST11.L) | C_{10}H_{8} | 128.169g/mol |
| 2    | 12.989 | 18.34  | Benzene Propanol           | C_{6}H_{12}O | 136.19g/mol   |
| 3    | 12.989 | 18.34  | Benzene Acetic Acid        | C_{6}H_{12}BrNO_{2} | 244.08g/mol |
| 4    | 24.527 | 13.93  | Furazan-3-Amine            | C_{2}H_{7}NO_{3} | 130.06g/mol |
| 5    | 25.238 | 14.07  | Pyrazole-4-Carboxylic acid | C_{6}H_{12}NO_{2} | 126.11g/mol |
| 6    | 25.892 | 8.49   | 2(3H) Furanone             | C_{6}H_{12}O | 84.07g/mol    |
Molecular docking was performed between compounds identified in Siddha medicine *Adathodai Kudineer* with targets SARS-CoV-2 Virus main protease and Spike protein bound with ACE2 receptor, the results of the binding affinity of these compound with their respective targets are given in (Table 2).

### Table 1: Phytocomponents identified in the Ethanolic extract of Medicinal compound *Adathodai Kudineer*

| S.No | RT   | Area % | Library/ID   | Mol. F | Mol. W (g/mol) |
|------|------|--------|--------------|--------|----------------|
| 1    | 5.259| 1.86   | Eucalyptol   | C10H16O | 154.25g/mol    |
| 2    | 5.259| 1.86   | Toluene      | C7H8   | 92.14g/mol     |
| 3    | 10.200| 11.06  | 2-Carene     | C10H16 | 136.23g/mol    |
| 4    | 10.622| 3.73   | Alpha-Copaene| C15H24 | 204.35g/mol    |
| 5    | 11.734| 3.32   | 1,6-Cyclodecadiene | C15H24 | 204.35g/mol |
| 6    | 11.907| 1.89   | Gamma-Murolene| C15H24 | 204.35g/mol    |
| 7    | 12.002| 3.36   | Beta-Copaene | C15H24 | 204.35g/mol    |
| 8    | 12.424| 43.10  | Cubebol      | C15H26O | 222.37g/mol   |
| 9    | 13.512| 3.07   | Selina-3,7 (11)-Diene | C15H24 | 204.35g/mol |
| 10   | 25.898| 3.65   | 2-Butanone   | C4H8O  | 72.11g/mol     |

### Table 2: Binding affinity of the compounds with their respective targets

| S.no | Compound name | PubChem ID | Binding energy for PDBID:6LU7 (KCal/mol) | Binding energyfor PDBID:6LZG (KCal/mol) |
|------|---------------|------------|----------------------------------------|----------------------------------------|
| 1    | Naphthalene   | 931        | -5.5                                   | -6.3                                   |
| 2    | Benzene Propanol | 31234     | -5.0                                   | -6.9                                   |
| 3    | Benzene Acetic Acid | 327550  | -5.9                                   | -6.9                                   |
| 4    | Furanan-3-Amine | 543119   | -4.6                                   | -5.2                                   |
| 5    | Pyrazol-4-Carboxylic acid | 643160 | -4.5                                   | -5.1                                   |
| 6    | 2(3H) Furanone | 140765   | -3.6                                   | -4.1                                   |
| 7    | Eucalyptol    | 2758       | -5.1                                   | -5.2                                   |
| 8    | Toluene       | 1140       | -4.2                                   | -5.4                                   |
| 9    | 2-Carene      | 78249      | -4.9                                   | -6.3                                   |
| 10   | Copaene       | 19725      | -5.9                                   | -6.5                                   |
| 11   | Alpha-Copaene | 70678558   | -8.2                                   | -10.9                                  |
| 12   | 1,6-Cyclodecadiene | 5365639 | -5.2                                   | -5.6                                   |
| 13   | Allomadendrene | 42608158 | -5.4                                   | -6.5                                   |
| 14   | Aromadendrene | 91354      | -6.5                                   | -7.0                                   |
| 15   | Gamma-Murolene | 12313020 | -5.9                                   | -8.0                                   |
| 16   | Beta-Copaene  | 87529      | -5.8                                   | -6.6                                   |
| 17   | Cubebol       | 11276107   | -6.6                                   | -7.4                                   |
| 18   | Selina-3,7 (11)-Diene | 522296 | -6.1                                   | -7.8                                   |
| 19   | 2-Butanone    | 6569       | 3.1                                    | -3.8                                   |
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| S. no | Compound name          | 3D Docking pose of compounds with target 6LU7 | 3D Docking pose of compounds with target 6LZG | 2D Plot of compounds with target 6LU7 | 2D Plot of compounds with target 6LZG |
|-------|------------------------|---------------------------------------------|---------------------------------------------|---------------------------------------|---------------------------------------|
| 1     | Naphthalene            | ![Image](image1.png)                        | ![Image](image2.png)                        | ![Image](image3.png)                  | ![Image](image4.png)                  |
| 2     | Benzene Propanol       | ![Image](image5.png)                        | ![Image](image6.png)                        | ![Image](image7.png)                  | ![Image](image8.png)                  |
| 3     | Benzene Acetic Acid    | ![Image](image9.png)                        | ![Image](image10.png)                       | ![Image](image11.png)                 | ![Image](image12.png)                 |
| 4     | Furazan-3-Amine        | ![Image](image13.png)                       | ![Image](image14.png)                       | ![Image](image15.png)                 | ![Image](image16.png)                 |
| 5     | Pyrazol-4-Carboxylic acid | ![Image](image17.png)   | ![Image](image18.png)                       | ![Image](image19.png)                 | ![Image](image20.png)                 |
| 6     | 2(3H) Furanone         | ![Image](image21.png)                       | ![Image](image22.png)                       | ![Image](image23.png)                 | ![Image](image24.png)                 |
| 7     | Eucalyptol             | ![Image](image25.png)                       | ![Image](image26.png)                       | ![Image](image27.png)                 | ![Image](image28.png)                 |
| 8     | Toluene                | ![Image](image29.png)                       | ![Image](image30.png)                       | ![Image](image31.png)                 | ![Image](image32.png)                 |
| 9     | 2-Carene               | ![Image](image33.png)                       | ![Image](image34.png)                       | ![Image](image35.png)                 | ![Image](image36.png)                 |
| 10    | Copaene                | ![Image](image37.png)                       | ![Image](image38.png)                       | ![Image](image39.png)                 | ![Image](image40.png)                 |
| 11    | Alpha-Copaene          | ![Image](image41.png)                       | ![Image](image42.png)                       | ![Image](image43.png)                 | ![Image](image44.png)                 |
| 12    | 1,6-Cyclodecadene      | ![Image](image45.png)                       | ![Image](image46.png)                       | ![Image](image47.png)                 | ![Image](image48.png)                 |
| 13    | Allomadendrene         | ![Image](image49.png)                       | ![Image](image50.png)                       | ![Image](image51.png)                 | ![Image](image52.png)                 |
| 14    | Aromadendrene          | ![Image](image53.png)                       | ![Image](image54.png)                       | ![Image](image55.png)                 | ![Image](image56.png)                 |
| 15    | Gamma-Muurolene        | ![Image](image57.png)                       | ![Image](image58.png)                       | ![Image](image59.png)                 | ![Image](image60.png)                 |
| 16    | Beta-Copaene           | ![Image](image61.png)                       | ![Image](image62.png)                       | ![Image](image63.png)                 | ![Image](image64.png)                 |
| 17    | Cubebol                | ![Image](image65.png)                       | ![Image](image66.png)                       | ![Image](image67.png)                 | ![Image](image68.png)                 |
| 18    | Selina-3,7(11)-Diene   | ![Image](image69.png)                       | ![Image](image70.png)                       | ![Image](image71.png)                 | ![Image](image72.png)                 |
| 19    | 2-Butanone             | ![Image](image73.png)                       | ![Image](image74.png)                       | ![Image](image75.png)                 | ![Image](image76.png)                 |
### Discussion

ACE2 receptors are used by SARS-CoV-2 in the entry of the target cells to cause Corona Viral Disease 19 in Humans (2). The above mentioned compounds present in the aqueous and ethanolic extract of *Adathodai kudineer* such as Naphthalene, Benzene Propanol, Benzene Acetic Acid, Furazan-3-amine, Pyrazol-4-Carboxylic acid, 2(3H) Furanone, Eucalyptol, Toluene, 2-Carene, Alpha-Copaene, 1,6-Cyclodecadiene, Aromadendrene, Gamma-murolene, Beta-copaene, Cubebol, Selina-3,7 (11) - Diene, 2-Butanonehaving minimum binding affinity against Spike protein (PDB ID 6LU7) and Spike protein ACE2 complex domain (PDB ID 6LZG) based on the molecular docking results. This indicates that there is a significant possibility of these molecules to inhibit the viral entry into target cellular pathway and replication. The exact mechanism behind this have to be studied further in various dimensions.

Molecular docking binding energy results and case report analysis on *Justicia adhatoda* L. leaves extract use for COVID 19 strongly recommended by researchers in prevention and treatment aspects (12)(13)(14). So, the therapeutic potency of this herbal present in AK will give a major impact for the treatment of SARS COV 2 infection. Research study confirms that the alcoholic extract of *Taxus baccata* has bronchodilator effect and can be able to decrease the bronchial hyper reactivity in experimental animals (15) The compound Glycyrrhizin present in the plant *Glycyrrhiza glabra* L. has antiviral effect. This plant has potent antiviral effect against Cytomegalo virus, SARS virus, Hepatitis A, B, C [16]. The Presence of Piperamides in the plant *Piper Longum* L. possess anti-viral against viruses related to upper respiratory tract infections and anti-proliferative effect (17).

![Figure 3: ADME Alpha Copaene](image-url)
Conclusion

The lead biomolecules which present in the Siddha drug Adathodai Kudineer such as Alpha-Copaene, Gamma-Muurolene, Selina-3,7 (11) – Diene, Cubebol, Aromadendrene have higher binding affinity towards the SARS-CoV-2 Spike Protein and ACE2 Receptor Spike protein Complex. Based on the findings of docking score values we can strongly suggest this Siddha poly herbal formulation Adathodai kudineer for the better management of COVID 19. Further preclinical and clinical trials have to be conducted in order to know the exact mechanism and efficacy of Adathodai Kudineer in SARS-CoV2 infection management.

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## Appendix

### Table 3: Physiochemical properties of active compounds of AdathodaiKudineer formulation predicted from SwissADME

| Sl. No | Molecule | Formula | MW | #Heavy atoms | #Aromatic heavy atoms | Fraction Csp3 | #Rotatable bonds | #H-bond acceptors | #H-bond donors | MR | TPSA |
|--------|----------|---------|----|--------------|----------------------|--------------|-----------------|------------------|----------------|-----|------|
| 1      | Naphthalene | C10H8 | 128.17 | 10 | 10 | 0 | 0.0 | 0 | 0 | 43.95 | 0 |
| 2      | Benzene Propanol | C9H12O | 136.19 | 10 | 6 | 0.33 | 3 | 1 | 1 | 42.18 | 20.23 |
| 3      | Benzene Acetic Acid | C9H10OBrNO2 | 244.09 | 13 | 6 | 0.22 | 3 | 3 | 2 | 53.53 | 63.32 |
| 4      | Furazan-3-Amine | C2H2N4O3 | 130.06 | 9 | 5 | 0 | 1 | 5 | 1 | 27.52 | 110.76 |
| 5      | Pyrazol-4-Carboxylic acid | C5H6N2O2 | 126.11 | 9 | 5 | 0.2 | 1 | 3 | 1 | 30.45 | 55.12 |
| 6      | 2(3H) Furanone | C4H6O2 | 84.07 | 6 | 0 | 0.25 | 0 | 2 | 0 | 20.04 | 26.3 |
| 7      | Eucalyptol | C10H18O | 154.25 | 11 | 0 | 1 | 0 | 1 | 1 | 47.12 | 9.23 |
| 8      | Toluene | C7H8 | 92.14 | 7 | 6 | 0.14 | 0 | 0 | 0 | 31.41 | 0 |
| 9      | 2-Carene | C10H16 | 136.23 | 10 | 0 | 0.8 | 0 | 0 | 0 | 45.22 | 0 |
| 10     | Copaene | C15H24 | 204.35 | 15 | 0 | 0.87 | 1 | 0 | 0 | 67.14 | 0 |
| 11     | Alpha-Copaene | C15H24 | 204.35 | 15 | 0 | 0.87 | 1 | 0 | 0 | 67.14 | 0 |
| 12     | 1,6-Cycloecdadiene | C10H16 | 136.23 | 10 | 0 | 0.6 | 0 | 0 | 0 | 47.12 | 0 |
| 13     | Allomadendrene | C15H24 | 204.35 | 15 | 0 | 0.87 | 1 | 0 | 0 | 67.14 | 0 |
| 14     | Aromadendrene | C15H24 | 204.35 | 15 | 0 | 0.87 | 1 | 0 | 0 | 67.14 | 0 |
| 15     | Gamma-Murolene | C15H24 | 204.35 | 15 | 0 | 0.73 | 1 | 0 | 0 | 69.04 | 0 |
| 16     | Beta-Copaene | C15H24 | 204.35 | 15 | 0 | 0.87 | 1 | 0 | 0 | 67.14 | 0 |
| 17     | Cubedol | C15H26O | 222.37 | 16 | 0 | 1 | 1 | 1 | 1 | 68.82 | 20.23 |

### Table 4: Lipophilicity of active compounds of AdathodaiKudineer formulation predicted from SwissADME

| Sl.No | Molecule | iLOGP | XLOGP3 | WLOGP | MLOGP | Silicos-IT Log P | Consensus Log P |
|-------|----------|-------|--------|--------|--------|-----------------|-----------------|
| 1     | Naphthalene | 1.99 | 3.3   | 2.84  | 4.26  | 3.11            | 3.1            |
| 2     | Benzene Propanol | 1.95 | 1.88  | 1.61  | 2.19  | 2.35            | 2              |
| 3     | Benzene Acetic Acid | 1.34 | -1.14 | 1.19  | -0.66 | 1.55            | 0.46           |
| 4     | Furazan-3-Amine | 0.31 | 0.12  | -0.43 | -1.45 | -1.42           | -0.57          |
| 5     | Pyrazol-4-Carboxylic acid | 0.81 | -0.24 | 0.12  | -0.4  | -0.26           | 0.01           |
| 6     | 2(3H) Furanone | 1.19 | 0.22  | 0.45  | -0.01 | 1.02            | 0.57           |
| 7     | Eucalyptol | 2.58 | 2.74  | 2.74  | 2.45  | 2.86            | 2.67           |
| 8     | Toluene | 1.85 | 2     | 2.73  | 3.52  | 2.44            | 2.51           |
| 9     | 2-Carene | 2.66 | 3     | 2.85  | 4.29  | 2.79            | 3.12           |
| 10    | Copaene | 3.4  | 4.27  | 4.47  | 5.65  | 3.73            | 4.3            |
| 11    | Alpha-Copaene | 3.4  | 4.27  | 4.47  | 5.65  | 3.73            | 4.3            |
| 12    | 1,6-Cycloecdadiene | 2.57 | 3.45  | 3.84  | 3.27  | 2.73            | 3.17           |
| 13    | Allomadendrene | 3.27 | 4.27  | 4.71  | 5.65  | 3.8             | 4.34           |
| 14    | Aromadendrene | 3.27 | 4.27  | 4.71  | 5.65  | 3.8             | 4.34           |
| 15    | Gamma-Murolene | 3.58 | 4.58  | 4.31  | 4.63  | 4.01            | 4.18           |
| 16    | Beta-Copaene | 3.35 | 4.27  | 4.71  | 5.65  | 4.01            | 4.4            |
| 17    | Cubedol | 3.09 | 3.47  | 3.92  | 3.81  | 3.22            | 3.5            |

### Table 5: Water solubility properties of all the active compounds of AdathodaiKudineer predicted from SWISS ADME

| ESOL Log S | ESOL Solubility (mg/ml) | ESOL Solubility (mol/l) | ESOL Class | All Log S | All Solubility (mg/ml) | All Solubility (mol/l) | All Class | Silicos-IT LogSwp | Silicos-IT Solubility (mg/ml) | Silicos-IT Solubility (mol/l) | Silicos-IT class |
|------------|-------------------------|-------------------------|------------|----------|------------------------|------------------------|-----------|------------------|--------------------------------|--------------------------------|-------------------------|
| -3.45      | 4.51E-02                | 3.52E-04                | Soluble    | -2.98   | 1.36E-01               | 1.06E-03               | Soluble   | -4.03           | 1.19E-02                        | 9.27E-05                         | Moderately soluble |
| -2.11      | 1.05E+00                | 7.68E-03                | Soluble    | -1.93   | 1.61E+00               | 1.18E-02               | Very soluble | -3              | 1.35E-01                        | 9.89E-04                         | Soluble |
| -0.78      | 4.06E+01                | 1.66E-01                | Very soluble | 0.3     | 4.89E+02               | 2.00E+00               | Highly soluble | -2.72          | 4.61E-01                        | 1.89E-03                         | Soluble |
| -1.07      | 1.11E+01                | 8.57E-02                | Very soluble | -2      | 1.30E+00               | 9.96E-03               | Soluble | 0.15            | 1.83E+02                        | 1.41E+00                         | Soluble |
| -0.82      | 1.93E+01                | 1.53E-01                | Very soluble | -0.46   | 4.38E+01               | 3.47E-01               | Very soluble | -0.13           | 9.37E+01                        | 7.43E-01                         | Soluble |
| -0.5       | 2.66E+01                | 3.16E-01                | Very soluble | -0.33   | 3.92E+01               | 4.66E-01               | Very soluble | -0.04           | 7.67E+01                        | 9.12E-01                         | Soluble |
| -2.52      | 4.63E+01                | 3.00E-03                | Soluble    | -2.59   | 3.98E-01               | 2.58E-03               | Soluble   | -2.45           | 5.45E-01                        | 3.33E-03                         | Soluble |
Table 6: Pharmacokinetic properties of all the active compounds of Adathodai Kudineer a classical Siddha herbal formulation

| Compound | GI absorption | BBB permeant | Pgp substrate | CYP1A2 inhibitor | CYP2C19 inhibitor | CYP2C9 inhibitor | CYP2D6 inhibitor | CYP3A4 inhibitor | log Kp (cm/s) |
|----------|---------------|--------------|---------------|------------------|------------------|------------------|------------------|------------------|-------------|
| -3.76    | Low           | Yes          | No             | Yes              | No               | No               | No               | No               | -4.2        |
| -4.01    | Low           | Yes          | No             | Yes              | No               | No               | No               | No               | -4.92       |
| -4.92    | Low           | Yes          | No             | Yes              | Yes              | Yes              | No               | No               | -4.2        |
| -4.92    | Low           | Yes          | No             | Yes              | Yes              | Yes              | No               | No               | -4.2        |
| -4.92    | Low           | Yes          | No             | Yes              | Yes              | Yes              | No               | No               | -4.87       |
| -4.92    | Low           | Yes          | No             | Yes              | Yes              | Yes              | No               | No               | -4.39       |
| -4.92    | Low           | Yes          | No             | Yes              | Yes              | Yes              | No               | No               | -6.53       |

Table 7: Drug likeliness of all the active compounds of Adathodai Kudineer predicted from SWISS ADME

| Lipinski #violations | Ghose #violations | Veber #violations | Egan #violations | Muegge #violations | Bioavailability Score |
|----------------------|-------------------|------------------|------------------|-------------------|----------------------|
| 1                    | 2                 | 0                | 0                | 2                 | 0.55                 |
| 0                    | 1                 | 0                | 0                | 2                 | 0.55                 |
| 0                    | 0                 | 0                | 0                | 0                 | 0.55                 |
| 0                    | 4                 | 0                | 0                | 2                 | 0.55                 |
| 0                    | 3                 | 0                | 0                | 1                 | 0.56                 |
| 0                    | 3                 | 0                | 0                | 2                 | 0.55                 |
| 0                    | 1                 | 0                | 0                | 2                 | 0.55                 |
| 0                    | 3                 | 0                | 0                | 2                 | 0.55                 |
| 1                    | 1                 | 0                | 0                | 2                 | 0.55                 |
| 1                    | 0                 | 0                | 0                | 1                 | 0.55                 |
| 1                    | 0                 | 0                | 0                | 1                 | 0.55                 |
| 1                    | 0                 | 0                | 0                | 1                 | 0.55                 |
Table 8: Medicinal chemistry properties of all the active compounds of *Adathodai* Kudineer predicted from SWISS ADME

| PAINS #alerts | Brenk #alerts | Leadlikeness #violations | Synthetic Accessibility |
|---------------|---------------|--------------------------|-------------------------|
| 0             | 0             | 1                        | 1                       |
| 0             | 0             | 1                        | 1                       |
| 0             | 1             | 1                        | 2.04                    |
| 0             | 2             | 1                        | 2.8                     |
| 0             | 0             | 1                        | 1.09                    |
| 0             | 0             | 1                        | 2.33                    |
| 0             | 0             | 1                        | 3.65                    |
| 0             | 0             | 1                        | 1                       |
| 0             | 1             | 1                        | 3.84                    |
| 0             | 1             | 2                        | 4.62                    |
| 0             | 1             | 2                        | 4.62                    |
| 0             | 1             | 2                        | 2.99                    |
| 0             | 1             | 2                        | 3.7                     |
| 0             | 1             | 2                        | 3.7                     |
| 0             | 1             | 2                        | 4.35                    |
| 0             | 1             | 2                        | 3.91                    |
| 0             | 0             | 2                        | 4.13                    |
| 0             | 1             | 2                        | 4.14                    |
| 0             | 0             | 1                        | 1                       |

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