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# In-silico studies of phytoconstituents of *Bacopa monnieri* and *Centella asiatica* with Crystal structure of Myelin Oligodendrocyte Glycoprotein against primary demyelination in Multiple Sclerosis

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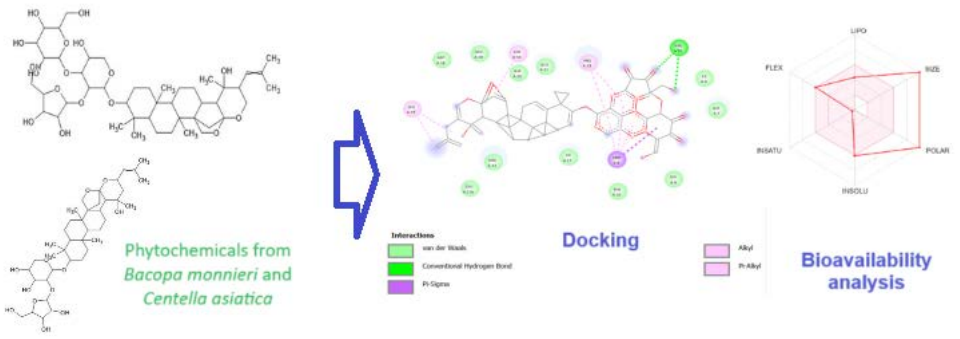
Article

## ABSTRACT




There is a rapid spread of Multiple Sclerosis disorder across the globe. There are around 2.8 million cases of Multiple Sclerosis in the world; among them, 1 million are just present in the US. Many drugs have been tested on MS patients but there is no effective treatment for MS till now. Many inhibitors, such as dronabinol, and nabilone, have been used to treat MS. So, we tested different compounds from *Bacopa monnieri and Centella asiatica* to inhibit the symptoms caused by MS. We targeted the 1PY9 receptor as it has shown some good results in experimental labs. In this article, we will study the binding interactions through the molecular docking model. Our study provided insight into possible treatments for MS during interactions between various bioactive compounds and MS receptors. This study found that Bacosine, Ursolic acid, Betulinic acid, Stigmastanol and Stigmasterol have the potential to inhibit the 1PY9 receptor and their binding energies are -10.12 kcal/mol, -9.52 kcal/mol, -8.95 kcal/mol, -9.93kcal/mol, and -9.51 kcal/mol. Based on bioavailability radar studies, Madecassic acid and Terminolic acid are two bioactive compounds that can be further used in Sclerosis disorders.

*Keywords: Multiple sclerosis, Bacopa monnieri, Centella asiatica, In-silico study, Myelin Oligodendrocyte Glycoprotein, Demyelination*

## INTRODUCTION

The central nervous system is affected by the chronic autoimmune illness known as Multiple sclerosis (MS). (CNS). The brain and spinal cord make up the central nervous system (CNS), which is in charge of carrying impulses throughout the body.[1] In MS, the immune system accidentally destroys the myelin that surrounds the CNS's nerve cells. This causes the myelin to develop scars (sclerosis), which interferes with the transmission of nerve signals.[2] The nerve filaments themselves may deteriorate over time, resulting in symptoms that are always present. Muscle weakness, balance issues, vision issues, and issues with thinking and remembering are just a few of the signs that MS can bring on.[3] The symptoms may be intermittent or persistent and can differ significantly from person to person. Although there is presently no cure for MS, there are several treatments that can help manage symptoms and halt the disease's progression.[4] A lot of research has focused on different methods that improve myelination, such as concentrating on specific signalling networks, stem cell therapy, etc.[5] Currently, the majority of MS therapy methods concentrate on reducing CNS inflammation. In 1993, interferon beta (IFN-beta) was first recognised as a successful therapy for multiple sclerosis.[6] Following that, medications for the treatment of MS were

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developed, including glatiramer acetate, natalizumab, alemtuzumab, and fingolimod.[7] All of the aforementioned medications were only mildly successful, and because of their notable side effects, they are not recommended for long-term use.[8]

*Bacopa monnieri* is an herbal extract made from the Brahmi plant, which has been used for thousands of years in traditional Ayurvedic treatment. It is thought to have a number of health advantages, including possible impacts on the nervous system. *Bacopa monnieri* has been shown in numerous studies to enhance age-related cognitive decline in healthy adults as well as memory, attention, and processing speed.[9] According to some studies, *Bacopa monnieri* may have anti-anxiety effects. It has long been used to help decrease stress and anxiety.[10] According to research, *Bacopa monnieri* has antioxidant and anti-inflammatory properties that may help shield the brain from oxidative stress and inflammation-related harm. It has been demonstrated that *Bacopa monnieri* increases synaptic activity in the brain, which may aid in improving memory and cognitive performance.[11]

*Centella asiatica*, also referred to as Gotu kola is a plant that has been used for therapeutic reasons in traditional medicine for thousands of years, especially in Asia. It is thought to have several health advantages, including possible impacts on the nervous system. More study is required to confirm the effects of *Centella asiatica* on memory and cognitive function, according to some studies.[12] According to some research, *Centella asiatica* may have anti-anxiety effects. It has been traditionally used to help lessen stress and anxiety. Antioxidant effects of *Centella asiatica* have been demonstrated; these effects may aid in protecting the brain from reactive stress and other types of harm.[13] It has been demonstrated that *Centella asiatica* increases blood flow, which may help to improve cognitive function and lower the chance of age-related cognitive decline.[14]

In order to research biological systems and address challenging biological problems computationally, the area of computational biology brings together computer science, statistics, mathematics, and biology.[15] A computational method called molecular docking is used to forecast how tiny molecules or ligands will bind to certain proteins.[16] It is a key tool in the drug development process because it enables scientists to find prospective drug candidates that have a high affinity and specificity for a given target protein. A mechanistic understanding of the interactions between tiny molecules or ligands can be gained by molecular docking.[17]

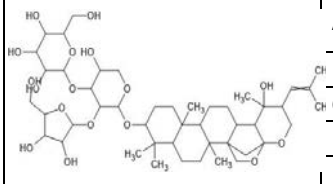
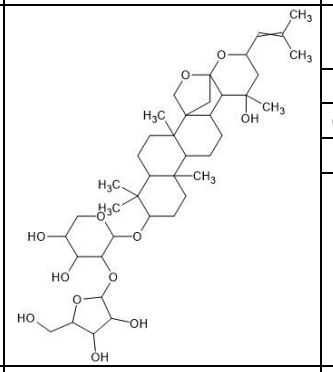
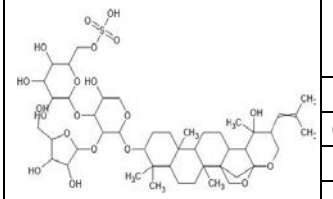
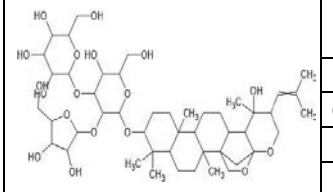
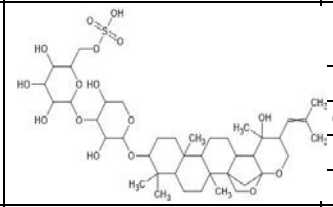
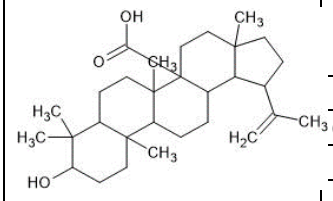
## RESULTS AND DISCUSSION

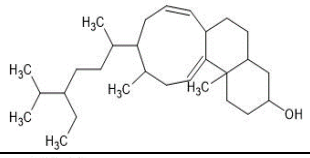
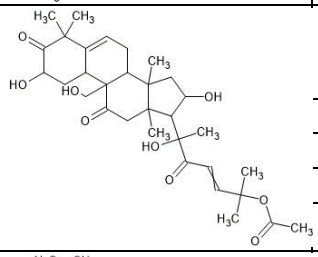
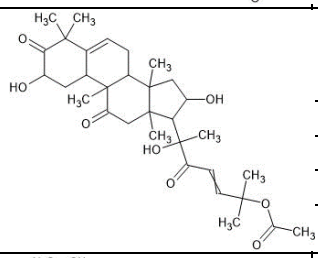
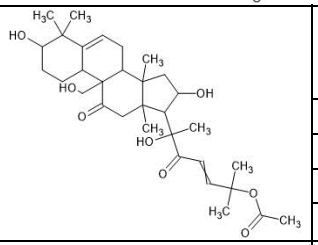
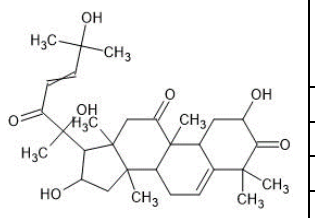
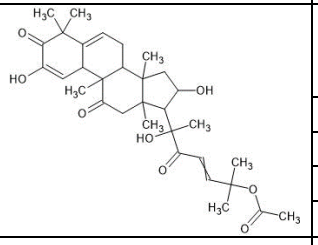
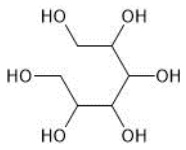
### ADME Analysis

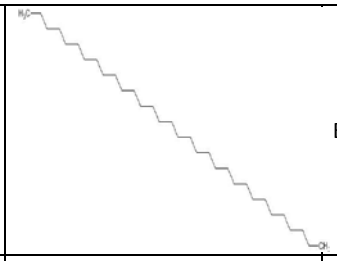
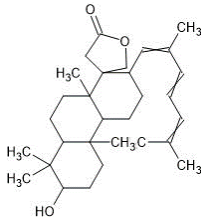
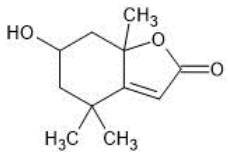
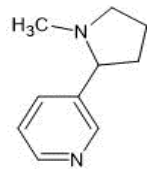
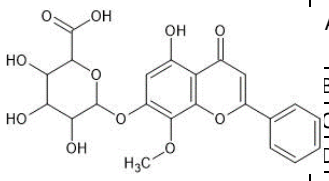
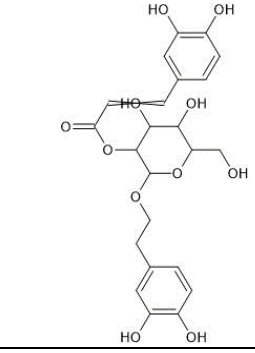
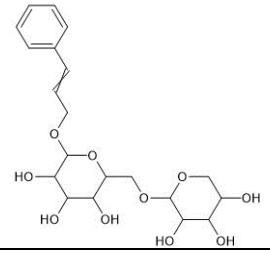
The bioactive components of *Bacopa monnieri* and *Centella asiatica* were subjected to Lipinski's law of five. Using physiochemical differences, we can remove compounds using this technique. All of the bioactive compounds in *Bacopa monnieri* and *Centella asiatica* revealed 0 to 3 violations, and all of the ligands were subjected to molecular docking. Compounds that violated the Lipinski rule were also taken. (SwissADME). All of the bioactive compounds were examined using the following 5 criteria, which are enumerated below:

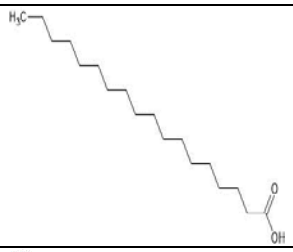
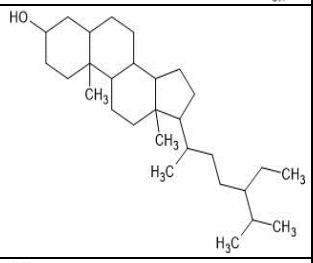
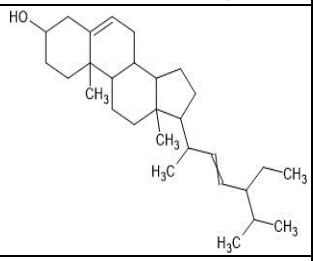
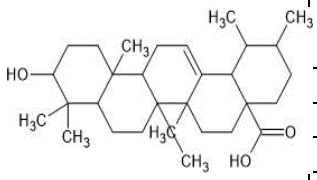
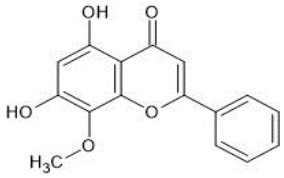
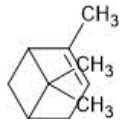
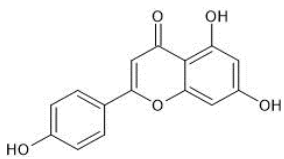
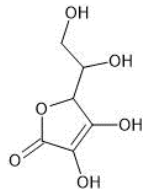
A. Molecular weight (< 500 Da) as A
B. Lipophilicity (LogP < 5) as B
C. H bond donor (< 5) as C
D. H bond acceptor (< 10) as D
E. Violations as E

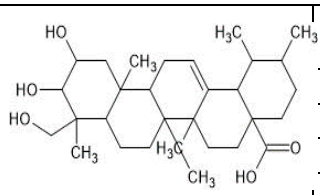
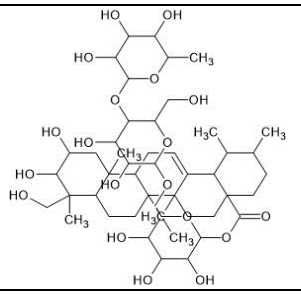
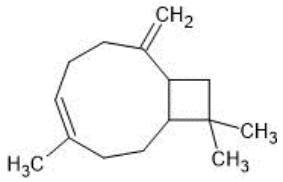
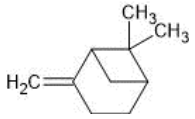
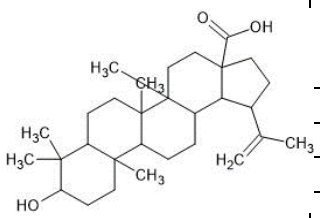
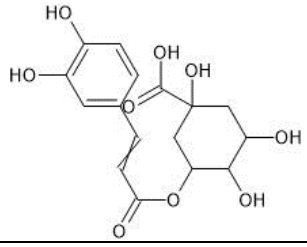
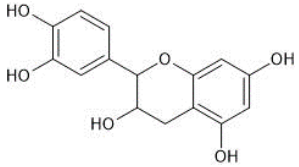
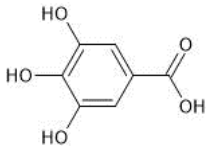
So, all these parameters of the specific compound are listed below in the table with the values of all the parameters:

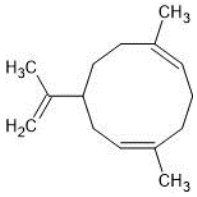
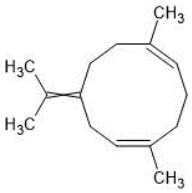
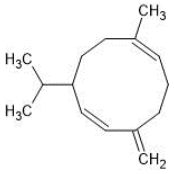
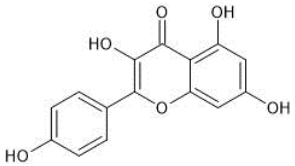
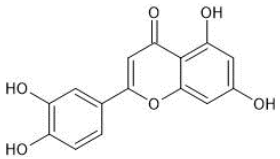
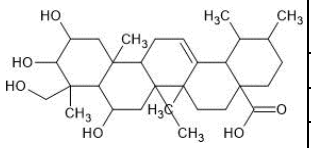
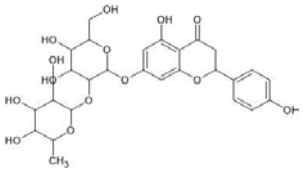
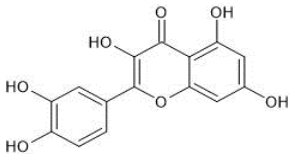
| Compound Name | Structure | Parameter | |
|---|---|---|---|
| Bacopasaponin C |  | A | 899.07 g/mol |
| | | B | 2.04 |
| | | C | 9 |
| | | D | 17 |
| | | E | 3 |
| Bacopasaponin G |  | A | 736.93 g/mol |
| | | B | 3.77 |
| | | C | 6 |
| | | D | 12 |
| | | E | 3 |
| Bacopaside I |  | A | 979.13 g/mol |
| | | B | 1.1 |
| | | C | 9 |
| | | D | 20 |
| | | E | 3 |
| Bacopaside II |  | A | 929.10 g/mol |
| | | B | 1.97 |
| | | C | 10 |
| | | D | 18 |
| | | E | 3 |
| Bacopaside III |  | A | 847.02 g/mol |
| | | B | 2.08 |
| | | C | 7 |
| | | D | 16 |
| | | E | 3 |
| Bacosine |  | A | 456.70 g/mol |
| | | B | 8.39 |
| | | C | 2 |
| | | D | 3 |
| | | E | 1 |
| Bacosterol | | A | 414.71 g/mol |

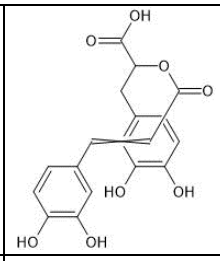
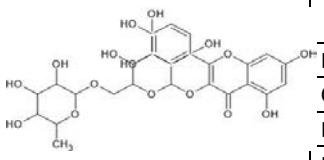
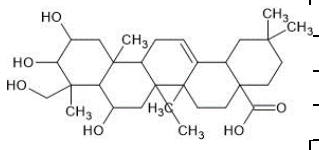
| | | | |
|---|---|---|---|
| |  | B | 9.34 |
| | | C | 1 |
| | | D | 1 |
| | | E | 1 |
| Cucurbitacin A |  | A | 574.70 g/mol |
| | | B | 1.97 |
| | | C | 4 |
| | | D | 9 |
| | | E | 1 |
| Cucurbitacin B |  | A | 558.70 g/mol |
| | | B | 2.64 |
| | | C | 3 |
| | | D | 8 |
| | | E | 1 |
| Cucurbitacin C |  | A | 560.72 g/mol |
| | | B | 2.82 |
| | | C | 4 |
| | | D | 8 |
| | | E | 1 |
| Cucurbitacin D |  | A | 516.67 g/mol |
| | | B | 2.06 |
| | | C | 4 |
| | | D | 7 |
| | | E | 1 |
| Cucurbitacin E |  | A | 556.69 g/mol |
| | | B | 3.25 |
| | | C | 3 |
| | | D | 8 |
| | | E | 1 |
| D-mannitol |  | A | 182.17 g/mol |
| | | B | -3.1 |
| | | C | 6 |
| | | D | 6 |
| | | E | 1 |
| Dotriacontane | | A | 450.87 g/mol |
| | | B | 16.95 |
| | | C | 0 |
| | | D | 0 |

| | | | |
|---|---|---|---|
| |  | E | 1 |
| Ebelin lactone |  | A | 454.68 g/mol |
| | | B | 8.2 |
| | | C | 1 |
| | | D | 3 |
| | | E | 1 |
| Loliolide |  | A | 196.24 g/mol |
| | | B | 1 |
| | | C | 1 |
| | | D | 3 |
| | | E | 0 |
| Nicotine |  | A | 162.23 g/mol |
| | | B | 1.17 |
| | | C | 0 |
| | | D | 2 |
| | | E | 0 |
| Oroxindin |  | A | 460.39 g/mol |
| | | B | 1.44 |
| | | C | 5 |
| | | D | 11 |
| | | E | 1 |
| Plantainoside B |  | A | 478.45 g/mol |
| | | B | 1.14 |
| | | C | 7 |
| | | D | 11 |
| | | E | 2 |
| Rosavin |  | A | 428.43 g/mol |
| | | B | -1.99 |
| | | C | 6 |
| | | D | 10 |
| | | E | 1 |

| | | | |
|---|---|---|---|
| Stearic acid |  | A | 284.48 g/mol |
| | | B | 8.23 |
| | | C | 1 |
| | | D | 2 |
| | | E | 1 |
| Stigmastanol |  | A | 416.72 g/mol |
| | | B | 8.32 |
| | | C | 1 |
| | | D | 1 |
| | | E | 1 |
| Stigmasterol |  | A | 412.69 g/mol |
| | | B | 8.56 |
| | | C | 1 |
| | | D | 1 |
| | | E | 1 |
| Ursolic acid |  | A | 456.70 g/mol |
| | | B | 7.34 |
| | | C | 2 |
| | | D | 3 |
| | | E | 1 |
| Wogonin |  | A | 284.26 g/mol |
| | | B | 3.49 |
| | | C | 2 |
| | | D | 5 |
| | | E | 0 |
| α-pinene |  | A | 136.23 g/mol |
| | | B | 4.48 |
| | | C | 0 |
| | | D | 0 |
| | | E | 1 |
| Apigenin |  | A | 270.24 g/mol |
| | | B | 3.02 |
| | | C | 3 |
| | | D | 5 |
| | | E | 0 |
| Ascorbic acid |  | A | 176.12 g/mol |
| | | B | -1.64 |
| | | C | 4 |
| | | D | 6 |
| | | E | 0 |

| | | | |
|---|---|---|---|
| Asiatic acid |  | A | 488.70 g/mol |
| | | B | 5.7 |
| | | C | 4 |
| | | D | 5 |
| | | E | 0 |
| Asiaticoside |  | A | 959.12 g/mol |
| | | B | 0.1 |
| | | C | 12 |
| | | D | 19 |
| | | E | 3 |
| β-caryophyllene |  | A | 204.35 g/mol |
| | | B | 4.38 |
| | | C | 0 |
| | | D | 0 |
| | | E | 1 |
| β-pinene |  | A | 136.23 g/mol |
| | | B | 4.16 |
| | | C | 0 |
| | | D | 0 |
| | | E | 1 |
| Betulinic acid |  | A | 456.70 g/mol |
| | | B | 8.21 |
| | | C | 2 |
| | | D | 3 |
| | | E | 1 |
| Chlorogenic acid |  | A | 354.31 g/mol |
| | | B | -0.42 |
| | | C | 6 |
| | | D | 9 |
| | | E | 1 |
| Cianidanol |  | A | 290.27 g/mol |
| | | B | 0.36 |
| | | C | 5 |
| | | D | 6 |
| | | E | 0 |
| Gallic acid |  | A | 170.12 g/mol |
| | | B | 0.7 |
| | | C | 4 |
| | | D | 5 |
| | | E | 0 |

| | | | |
|---|---|---|---|
| Germacrene A |  | A | 204.35 g/mol |
| | | B | 5.87 |
| | | C | 0 |
| | | D | 1 |
| | | E | 1 |
| Germacrene B |  | A | 204.35 g/mol |
| | | B | 5.77 |
| | | C | 0 |
| | | D | 0 |
| | | E | 1 |
| Germacrene D |  | A | 204.35 g/mol |
| | | B | 4.74 |
| | | C | 0 |
| | | D | 0 |
| | | E | 1 |
| Kaempferol |  | A | 286.24 g/mol |
| | | B | 1.9 |
| | | C | 4 |
| | | D | 6 |
| | | E | 0 |
| Luteolin |  | A | 286.24 g/mol |
| | | B | 2.53 |
| | | C | 4 |
| | | D | 6 |
| | | E | 0 |
| Madecassic acid |  | A | 504.70 g/mol |
| | | B | 4.36 |
| | | C | 5 |
| | | D | 6 |
| | | E | 1 |
| Naringin |  | A | 580.53 g/mol |
| | | B | -0.44 |
| | | C | 8 |
| | | D | 14 |
| | | E | 3 |
| Quercetin |  | A | 302.24 g/mol |
| | | B | 1.54 |
| | | C | 5 |
| | | D | 7 |
| | | E | 0 |

| | | | |
|---|---|---|---|
| Rosmarinic acid |  | A | 360.31 g/mol |
| | | B | 2.36 |
| | | C | 5 |
| | | D | 8 |
| | | E | 0 |
| Rutin |  | A | 610.52 g/mol |
| | | B | -0.33 |
| | | C | 10 |
| | | D | 16 |
| | | E | 3 |
| Terminolic acid |  | A | 504.70 g/mol |
| | | B | 4.5 |
| | | C | 5 |
| | | D | 6 |
| | | E | 1 |

**Molecular Docking**

47 bioactive compounds are subjected to the docking process. Molecular docking is one of the power takes of bioinformatics. This tool is very helpful in visualizing the docking of ligands to proteins and thus a complex of ligands and proteins is formed and gives us the binding energy values. All the data that we obtain through the process of docking is used for drug discovery. Bacopasaponin C, which is one of the bioactive molecules, had the lowest binding energy value of all of them at -13.34 kcal/mol, followed by Bacopaside III, which had a binding energy value of -12.42 kcal/mol.

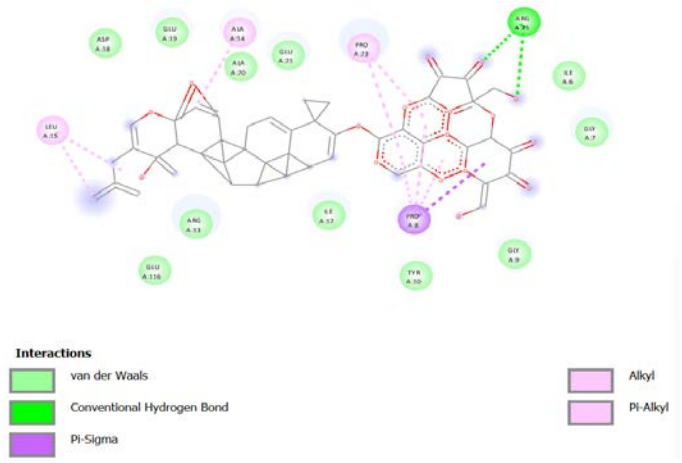
**Table 2:** Results of molecular docking of 47 ligands from *Bacopa monnieri and Centella asiatica* 1PY9 using Autodock 4.2

| **Ligands** | Binding Energy (ΔG)(kcal/mol) | **Ligand Efficiency** | **Inhibition Constant (µM)** | Intermolecular Energy (kcal/mol) | Vdw H-bond desolvation (kcal/mol) |
|---|---|---|---|---|---|
| **Bacopasaponin C** | **-13.34** | **-0.21** | **166.06** | **-15.43** | **-14.85** |
| Bacopasaponin G | -6.59 | -0.13 | -14.86 | -10.17 | -9.82 |
| Bacopaside I | -5.69 | -0.08 | 68.02 | -11.65 | -8.82 |
| Bacopaside II | -4.41 | -0.07 | 583.66 | -10.38 | -9.88 |
| **Bacopaside III** | **-12.42** | **-0.21** | **790.59** | **-14.8** | **-9.57** |
| **Bacosine** | **-10.12** | **-0.31** | **37.98** | **-11.32** | **-5.83** |
| Bacosterol | -7.92 | -0.26 | 1.56 | -10.01 | -9.61 |
| Cucurbitacin A | -7.36 | -0.18 | 4.02 | -10.64 | -10.1 |
| Cucurbitacin B | -8.2 | -0.2 | 975.23 | -10.88 | -10.22 |
| Cucurbitacin C | -6.74 | -0.17 | 11.54 | -10.02 | -9.6 |
| Cucurbitacin D | -6.87 | -0.19 | 9.22 | -9.26 | -9.13 |

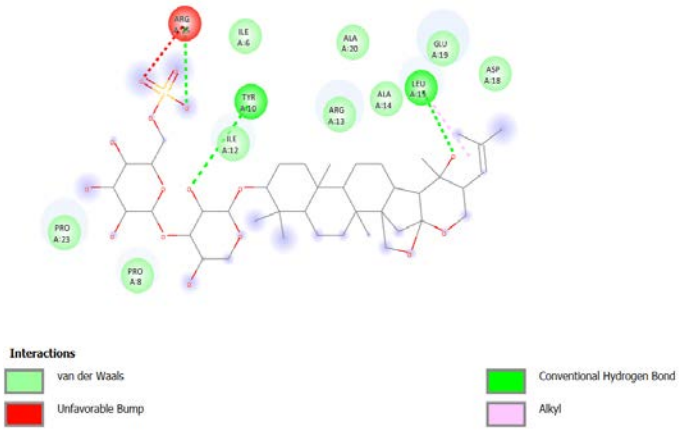
| | | | | | |
|---|---|---|---|---|---|
| Cucurbitacin E | -7.14 | -0.18 | 5.8 | -9.83 | -9.24 |
| D mannitol | -2.13 | -0.18 | 27.62 | -5.41 | -4.92 |
| Dotriacontane | -2.71 | -0.08 | 10.38 | -11.36 | -11.36 |
| Ebelin lactone | -8.27 | -0.25 | 868.05 | -9.46 | -9.56 |
| Loliolide | -5.23 | -0.37 | 147.9 | -5.52 | -5.31 |
| Nicotine | -5.05 | -0.42 | 198.77 | -5.35 | -4.3 |
| Oroxindin | -7.64 | -0.23 | 2.52 | -10.62 | -7.29 |
| Plantainoside B | -4.28 | -0.13 | 727.03 | -9.05 | -8.57 |
| Rosavin | -4.56 | -0.15 | 455.71 | -8.44 | -7.77 |
| Stearic acid | -5.84 | -0.29 | 52.65 | -10.91 | -7.49 |
| Stigmastanol | -8.95 | -0.3 | 276.74 | -11.03 | -11.08 |
| **Stigmasterol** | **-9.51** | **-0.32** | **107.16** | **-11.3** | **-11.28** |
| **Ursolic acid** | **-9.52** | **-0.29** | **105.1** | **-10.42** | **-5.1** |
| Wogonin | -5.44 | -0.26 | 103.5 | -6.63 | -6.53 |
| α-pinene | -4.3 | -0.43 | 705.87 | -4.3 | -4.32 |
| Apigenin | -6.24 | -0.31 | 26.58 | -7.44 | -7.13 |
| Ascorbic acid | -4.01 | -0.33 | 1.15 | -5.8 | -5.33 |
| Asiatic acid | -7.81 | -0.22 | 1.88 | -9.6 | -8.17 |
| Asiaticoside | -4.84 | -0.07 | 281.63 | -11.41 | -10.98 |
| β-caryophyllene | -5.64 | -0.38 | 74.02 | -5.64 | -5.63 |
| β-pinene | -4.43 | -0.44 | 566.62 | -4.43 | -4.41 |
| **Betulinic acid** | **-9.93** | **-0.3** | **52.42** | **-11.13** | **-6.82** |
| Chlorogenic acid | -6.48 | -0.26 | 17.83 | -9.76 | -5.14 |
| Cianidanol | -6.07 | -0.29 | 35.7 | -7.86 | -7.13 |
| Gallic acid | -6.81 | -0.57 | 10.22 | -8.3 | -2.82 |
| Germacrene A | -5.52 | -0.37 | 90.57 | -5.81 | -5.73 |
| Germacrene B | -5.36 | -0.36 | 118.07 | -5.36 | -5.41 |
| Germacrene D | -5.38 | -0.36 | 113.96 | -5.68 | -5.62 |
| Kaempferol | -5.94 | -0.28 | 44.51 | -7.43 | -7.09 |
| Luteolin | -5.99 | -0.29 | 40.9 | -7.48 | -6.95 |
| Madecassic acid | -8.4 | -0.23 | 690.89 | -10.49 | -5.23 |
| Naringin | -5.96 | -0.15 | 42.8 | -10.14 | -9.52 |
| Quercetin | -5.74 | -0.26 | 61.64 | -7.53 | -7.37 |
| **Rosmarinic acid** | **-8.53** | **-0.33** | **559.78** | **-12.11** | **-6.7** |
| Rutin | -4.46 | -0.1 | 536.21 | -9.23 | -8.59 |
| **Terminolic acid** | **-8.88** | **-0.25** | **308.15** | **-10.97** | **-5.5** |

**Interactions**

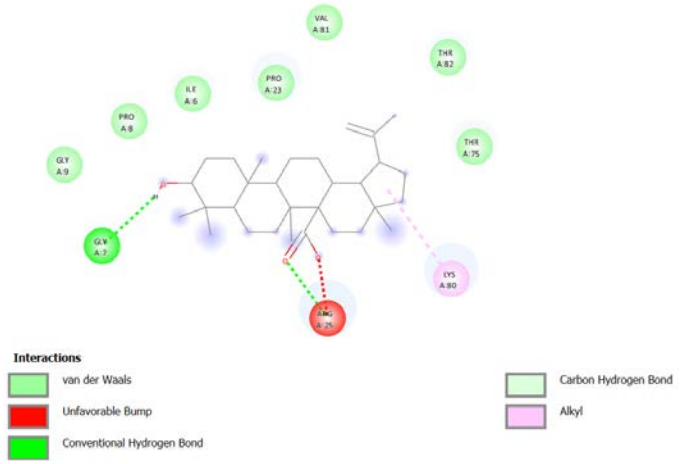
Represents the 2D interactions between the key bioactive compounds with the Crystal structure of MOG (PDB ID: 1PY9) with the help of BIOVIA Discovery Studio.




***A. Interaction between Bacopasaponin C and MOG receptor:*** Among the 20 conformations of Bacopasaponin C, −13.34 kcal/mol , the least binding energy that was measured. Five various contact patterns were noticed: van der Waals, Conventional hydrogen bond, alkyl, pi-alkyl and Pi-sigma bonds.

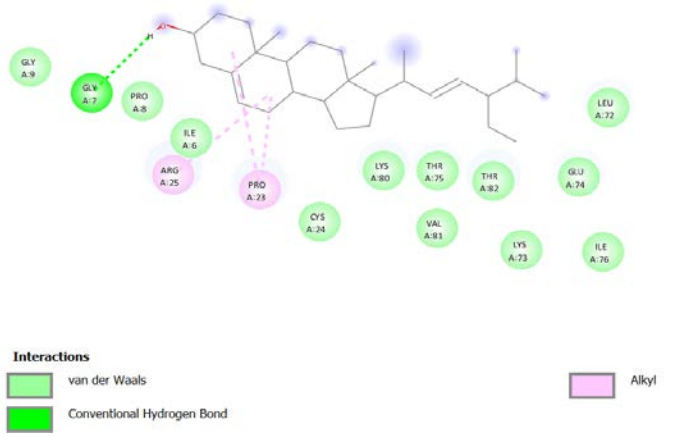



B. **Interaction between Bacopaside III and MOG receptor:** Among the 20 conformations of Bacosine, − 10.12 kcal/mol, the least binding energy that was measured. Five various contact patterns were noticed: van der Waals, Conventional hydrogen bond, alkyl, and Carbon hydrogen bond and an unfavourable bump

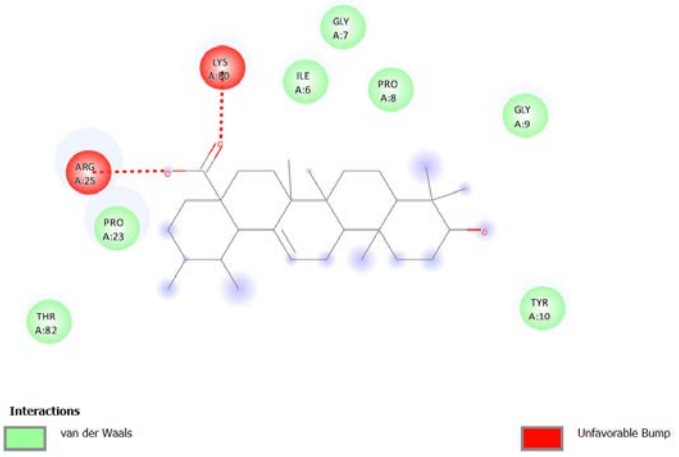



**C. Interaction between Bacosine and MOG:** Among the 20 conformations of Bacosterol, − 7.92 kcal/mol, the least binding energy that was measured. Four various forms of contact were noticed,

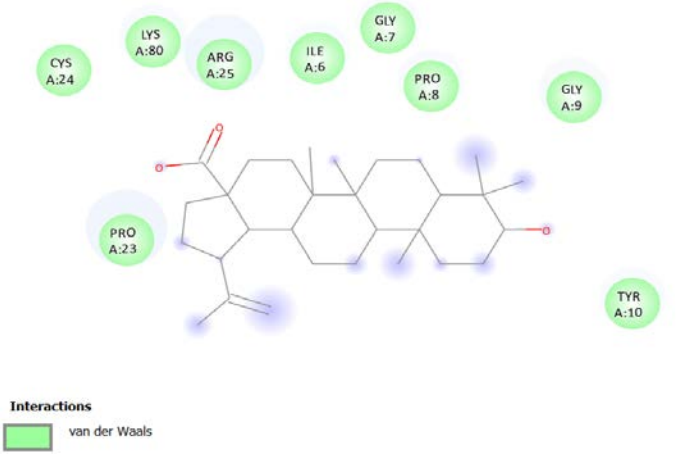
including van der Waals, Conventional hydrogen bond, alkyl bond and an unfavourable bump.



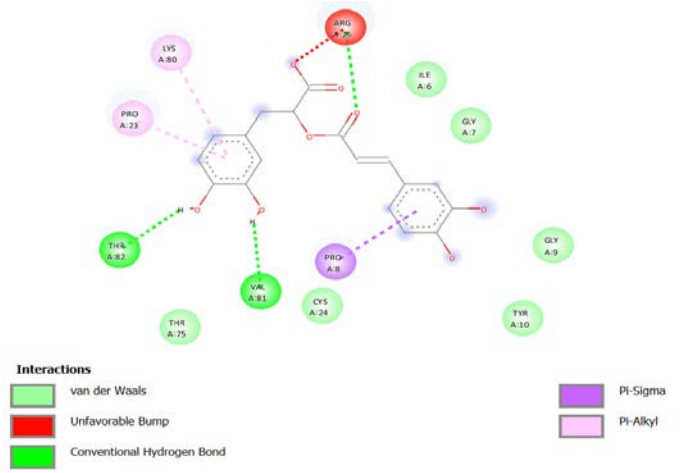

D. Interaction between Stigmasterol and MOG receptor: Among the 20 confirmations of Ursolic acid – 9.52 kcal/mol. The least binding energy that was measured. Five various forms of contact were noticed, including van der waals and an unfavourable bump.




***E. Interaction between Ursolic acid and MOG receptor:*** Among the 20 conformations of Wogonin, − 5.44 kcal/mol, the least binding energy that was measured. Five various contact patterns were noticed: van der Waals, Conventional hydrogen bond, Pi-alkyl, Pi-Donor hydrogen bond and Pi-Lone pair.

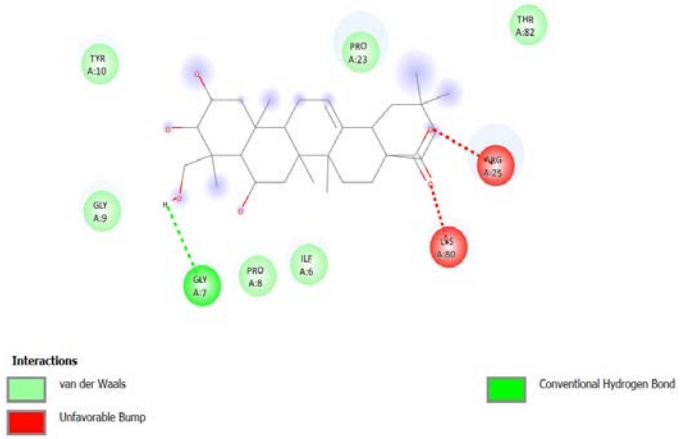



***F. Interaction between* Betulinic acid *and MOG receptor:*** Among the 20 conformations of Cholorgenic acid, − 6.48 kcal/mol, the least binding energy that was measured. Five various contact patterns were noticed: van der Waals, Conventional hydrogen bond, Pi-alkyl, and Pi-Anion and an unfavourable bump.




***G. Interaction between* Rosmarinic acid *and 1PY9 receptor***

Among the 20 conformations of Rutin, − 4.46 kcal/mol, the least binding energy that was measured. Five various forms of contact were noticed, including van der Waals, Conventional hydrogen bond, Pi-alkyl, Pi-sigma and Carbon hydrogen bond.




***H. Interaction between* Terminolic acid *and 1PY9 receptor:*** Among the 20 conformations of Terminolic acid, − 8.88 kcal/mol, the least binding energy that was measured. Three various forms of contact were noticed, including van der Waals, and Conventional hydrogen bond and an unfavourable bump.

**Figure 1**: Characterize the 2D representations of the 8 key bioactive compounds that have been selected and screened after the docking process and obtained the 2d interaction of them through the use of BIOVIA Discovery studio for the better understanding of the bonds that have been made and at which site the compounds have interacted with the receptor.

**Bioavailability Radar**

Furthermore, the analysis includes ligands and a study was done using bioavailability radar. It is used to look into the ligands' drug likeliness, which is established on 6 properties. Studies showed that some ligands were orally available as some fitted the radar's pink pink-shaded region. So, some of the selected ligands are orally bioavailable and some should be given in some other form.

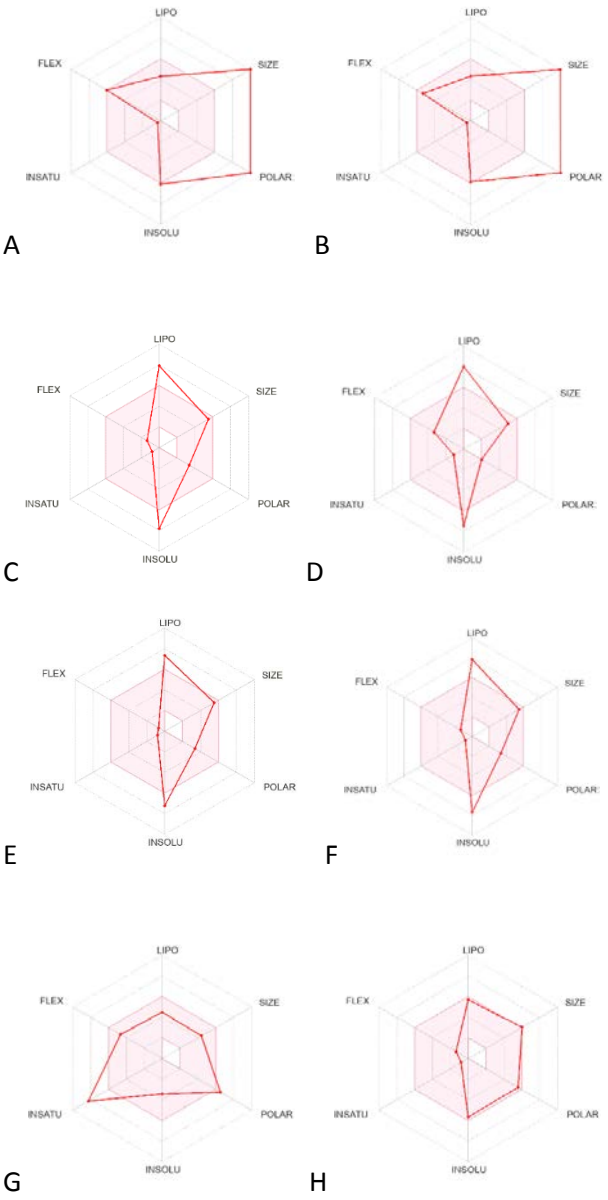



**Figure 2**: Represents drug-likeliness of 8 key bioactive compounds. The pink-shaded zone is an estimated physicochemical space for oral bioavailability. LIPO (Lipophility): − 0.7 < XLOGP3 < + 5.0. SIZE: 150 g/mol < MV < 500 g/mol. POLAR (Polarity: 0 < LogS (ESOL) < 6. INSATU (Insaturation): 0.25 < fraction Csp3 < 1. FLEX (Flexibility): 0 < Number of rotatable bonds < 9): 20Å$^2$ < TPSA < 130Å$^2$. INSOLU (Insolubility). (A) Bacopasaponin C (B) Bacopaside III (C) Bacosine (D) Stigmasterol (E) Ursolic acid (F) Betulinic acid (G) Rosmarinic acid (H) Terminolic acid.

### BOILED-Egg

BOILED-Egg was checked for all the 47 bioactive compounds and it showed the worst results as all the molecules were not able to cross the gastrointestinal tract only and many of them were out of range but some of them were also able to cross the Blood-Brain Barrier. We can say this by seeing the boiled eggs as the molecules present within the white portion and some in the yellow portion.

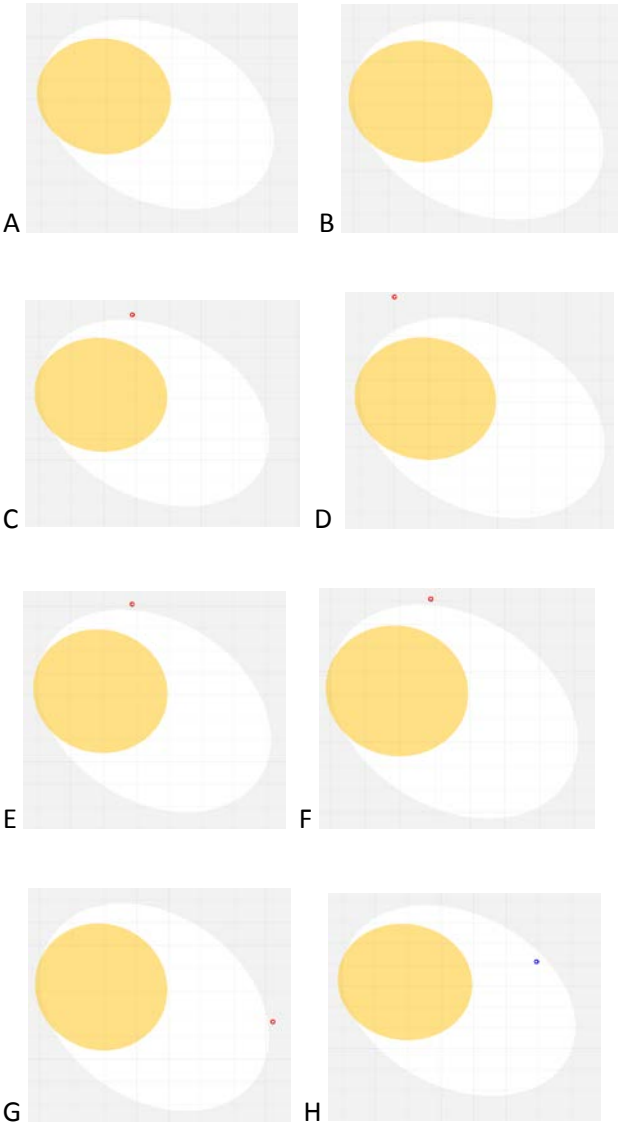



**Figure 3:** BOILED-Egg of 8 key selected bioactive compounds. Molecules in the yellow portion show that they can cross BBB and molecules in the white region showed that molecules can cross the gastrointestinal tract and the remaining ones are out of range. (A) Bacopasaponin C (B) Bacopaside III (C) Bacosine (D) Stigmasterol (E) Ursolic acid (F) Betulinic acid (G) Rosmarinic acid (H) Terminolic acid. These figures have been obtained through the use of SwissADME.

## EXPERIMENTAL

### Ligand Selection

We will be using *Bacopa monnieri* and *Centella asiatica*, known for their uses in healthcare. Several research papers have been studied to get the data about bioactive compounds of *Bacopa monnieri and Centella asiatica.* A total of 47 bioactive compounds were used for this study. These bioactive compounds are taken from *Bacopa monnieri*[18-19] *and Centella asiatica.*[20-21] The compounds which were extracted from this plant are used in molecular docking. The structures are downloaded in .sdf format from PubChem databank, but docking is only possible in .pdb format so all the extensions were changed to .pdb files with the use of PyMol software.

**Receptor**

The study's receptor is 1PY9, an MS autoantigen crystal structure. The RCSB PDB data archive was used to download the 3D structure of the receptor in PDB format. The PDB format is then converted to pdbqt format for docking purposes.[22]

**ADME Analysis Test**

The initial screening of ligands was conducted using a web-based programme named SwissADME.[23] Molecular weight 1.500 Da, high lipophilicity, Log P value 5, hydrogen bond donors 5, and hydrogen acceptors 10 are the five factors examined by this test. Ligand violation denotes that the drug is unfit for production, which is carried out by Lipinski's regulation.[24]

**Molecular Docking**

For obtaining protein-ligand complexes, use Autodock 4.2. Prior to molecular docking, the autoantigen underwent processing and optimisation. The removal of inhibitor molecules was done distantly by the receptor first.[25] Polar hydrogens, Kollman charges, and Gasteiger charges were also included. In order to ensure that the ligand binding position is not restricted to a particular region, the protein molecule was engulfed within a grid box. Following the docking procedure, a DLG file is produced in which the binding energies of various docking locations are determined in a total of 20 conformations in each ligand. The ligand shape with the lowest binding energy is chosen.[26-30]

**Bioavailability Radar**

The SwissADME tool is used to analyse the drug likelihood of different cannabinoids with binding energies lower than the control, after which six properties are taken into consideration to create a bioavailability radar. The six factors we take into account are solubility, size, lipophilicity, polarity, flexibility, and saturation. The pink-shaded area indicates the optimal values of the six parameters, and any deviation from these regions indicates that the ligand should not be orally bioavailable.[24]

**BOILED-Egg**

At various stages of drug discovery, gastrointestinal adsorption and brain access are two pharmacokinetic behaviours of critical significance. Calculating the polarity and lipophilicity of small molecules is how the BOILED-Egg, also known as the Brain or IntestinaL Estimated Permeation Method, functions as an accurate predictive model. Physical-chemical descriptors are used to derive predictions of both gut and brain penetration, which are then converted into molecular designs created by models that are quick to run, conceptually simple, and accurate. There are numerous uses for boiled eggs. It is helpful for drug development's early-stage library filtering through the final assessment. It is acquired using the SwissADME instrument.[24]

Boiling eggs contain molecules called "dots" in the yolk that are thought to passively penetrate the blood-brain barrier. It is expected that the molecules in cooked egg white's "dots" passively permeate the digestive system. The CNS is expected to bind to the molecules in blue dots via P-glycoprotein. Red dots indicate molecules for which P-glycoprotein association with the CNS is not expected.[23]

## CONCLUSION

In this study, 47 bioactive compounds were screened from *Bacopa monnieri* and *Centella asiatica*. The compounds were first screened using Lipinski's rule of five to examine the drug probability of the compound. Some of the compounds were drug-friendly and subsequently underwent molecular docking. We then analyzed the docking results and found that Bacopasaponin C and Bacopaside III were the most useful in terms of binding energy. All the ligands were then run on the bioavailability radar and some of them passed the result with some compounds fitting the pink-shaded region. Second, when targeting multiple sclerosis, it was important to check boiled eggs for all compounds. This study showed that only some compounds crossed the BBB which concludes that *Bacopa monnieri and Centella asiatica* is a good choice to treat neurological disorders.

Phytocompounds obtained from Bacopa monnieri and Centella asiatica can be of great choice because of its unique properties and their tendency to cross the Blood Brain Barrier. To check the importance of these phytocompounds with more accuracy and efficiency molecular dynamics simulations can be done in future studies. Due to limited facilities only, molecular docking has been done till now. Experimental studies in lab and further clinical trials will provide us with accurate data further.

## CONFLICT OF INTEREST

The authors declare there is no conflict of interest for publication of this work.

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