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DEMENTIA DISEASE DETECTION APPLICATION AND ESTABLISHING NOVEL DRUG LEADS FOR SYPHILIS CAUSING DEMENTIA

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ABSTRACT

Neuro-syphilis is a neurological condition in which brain cell death results in memory loss and cognitive deterioration. The dementia, which is a neurodegenerative form, begins mildly and worsens over time. Brain image analysis, which produces results to identify brain illnesses, is a significant area of medical research. Low brain activity and blood flow are the key contributors of neuro-syphilis. In general, medical images are segmented using this technique. The hippocampal region of the brain is a crucial part. Human behaviour is often determined by the hippocampal function. It takes many hours for an expert to manually segment the hippocampus. Additionally, Syphilis is now known to be a bacterial condition that is typically transferred through sexual intercourse. The condition often begins as a painless sore on the mouth, genitalia, or rectum. Syphilis spreads by skin or mucous membrane contact with these lesions.

In image processing there are various techniques available for segmentation process. In this work a modified approach based on the watershed algorithm is used for segmenting the hippocampus region. The brain images converted into binary form using two approaches. The first approach is block mean, mask and labelling concepts and in the second approach top hat, mask and labelling concepts. However it is found that some part of the image contains holes which interrupt the segmentation process. In recent years, digital medical imaging technology has opened its door to the community. In this work we detect the brain abnormalities in Syphilis.

The proposed technique will use the MRI slices to create a 3D model of the brain. This approach is more precise and dependable. Different techniques are applied to MRI slices, including denoising, segmentation, slice-o-matic (3D creation), and estimation of the residual volume of the various brain regions. The ratio of grey to white matter is used to assess a person's susceptibility to syphilis.

In brain MRI, the damaged area is highlighted via image segmentation. In a brain MRI, the hippocampus and overall brain volume are the areas that are diagnosed. Studies have shown that the plants *Taxillus chinensis*, *Carica papaya*, *Ranunculus bulbosus*, *Peltophorum africanum*, *Panax notoginseng*, etc. play an important role in the treatment of parasitic and infectious diseases including Syphilis. 3d structure of the bacterial receptor is modelled using homology modelling. HTS is performed on the phytocompounds of the above plants. As per HTS it is seen that Pinocembrin docks best with the viral receptor and hence they can be used as novel drug leads for the disorder.

Keywords: ***Neuro-syphilis, cognitive decline, pre-processing, homology modelling, ADME, HTS***.

INTRODUCTION

Dementia

Dementia states the state of a person's mental and cognitive function and always may not be related with any specific disease. Person with dementia may have one or many specific difficulties like a decline in memory, reasoning, language, coordination, mood and behaviour among others. One of the characteristic seen in neurosyphilis patent is dementia [1].

Disease etiology

A progressive neurological condition is neurosyphilis disease. It results in an irreversible loss of neurons and a decline in mental faculties, such as memory and thinking, severe enough to interfere with social or professional functioning. Neurotransmitters, important brain chemicals involved in transmitting messages in the brain, are shown to be insufficient in patients. A rare type of dementia is neurosyphilis illness. There is currently no treatment for neurosyphilis, however, there are techniques to halt the disease's progression and assist patients with some symptoms. Given that it is fatal and incurable, neurosyphilis is considered a terminal illness [2, 3].

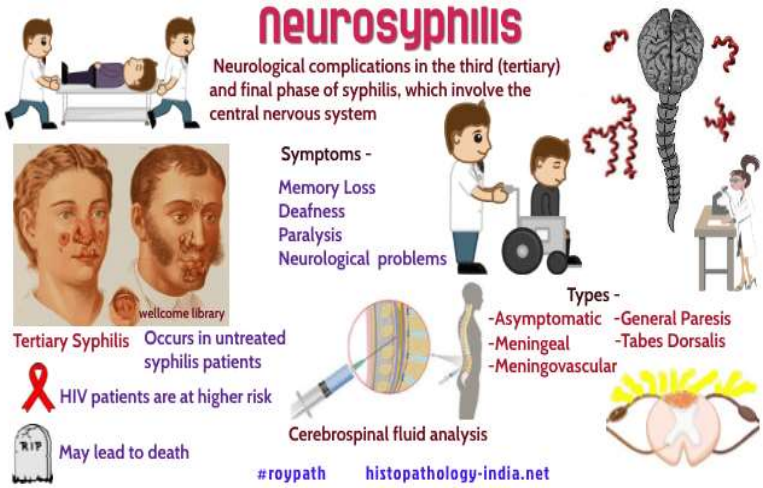


Fig. 1: Neurological complications in syphilis [figure adapted from http://www.histopathology-india.net/NeuSyp.htm]

Neurosyphilis:

A illness affecting the brain's surface, the brain itself, or the spinal cord called neurosyphilis. People with syphilis may experience it, particularly if they are not treated.

One of the effects of late syphilis is dementia, which is characterised by cognitive decline and behavioural issues. Neurosyphilis-related cognitive deterioration, behavioural disturbance, hyperactivity, hallucinations, short-term memory loss, and Argyll Robertson student [3].

Paretic neurosyphilis, also known as dementia paralytica, generalised paralysis, or general paresis, is the most common cause of syphilitic dementia. About 5% of people with early syphilis who are not treated develop paretic neurosyphilis, often 10 to 25 years after the infection [4].

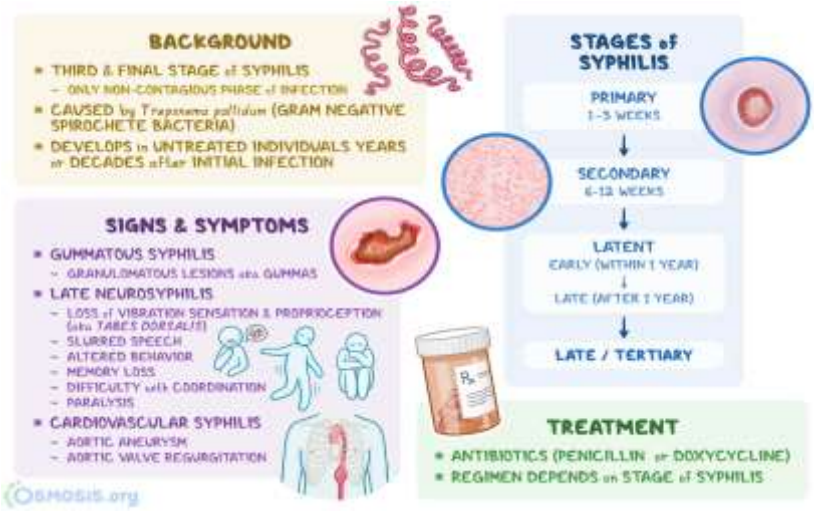


Fig. 2: Neurosyphilis: signs & symptoms [figure adapted from https://anypics.homes/syphilis-bacteria-name]

Risk Factors

The greatest risk factor for neurosyphilis disease is its terminal stage, but Dementia is not a typical part of aging since most people with neurosyphilis disease are diagnosed at age 42. It is also seen that people younger than 42 develops the disease but rarely [4, 5].

High-Throughput Screening (HTS)

The process of high-throughput screening (HTS) is used to find chemical and biologically active substances. HTS is currently becoming more and more popular in the pharmaceutical sectors. Additionally, it is utilised to characterise toxicological, pharmacokinetic, and metabolic information about novel medications at a significantly lower cost. HTS comprises several steps including Target Recognition, Homology Modelling, Model Evaluation, Ligand Selection and Retrieval from PubChem. Further using Lipinski's rule of five we find the drug-like properties'. further docking is performed. The goal of HTS is to select novel biological active compounds from various natural products [6, 7].

Medicinal plants & the properties

1. *Taxillus chinensis*

T. chinensis has been found to have anti-inflammatory, antioxidant, antihypertensive, antihyperglycemic, and other neurological characteristics, according to pharmacological tests. Traditional anti-cancer and neurological preparations use taxillus [8].

2. *Carica papaya*

The antioxidant benefits of carica papaya leaf in neurodegenerative diseases like neurosyphilis are further supported by the leaf's high degree of antioxidant activity against and spatial memory loss [9].

3. *Peltophorum africanum*

Antioxidants found in peltophorum can be used to treat neurological diseases. They reduce the course of neuronal cell loss and have neuroprotective (preventing apoptosis) and neuroregenerative roles by reducing or correcting cellular damage [11].

4. *Ranunculus bulbosus*

For skin conditions, arthritis, gout, nerve pain, flu (influenza), swine flu, and meningitis, use bulbous buttercup (Ranunculus bulbosus). Aconitine, the main active ingredient, has cardiotoxic and neurotoxic properties [12].

5. *Panax notoginseng*

Saponins from Panax have been traditionally used as a medication in China for hundreds of years because of their magical medical potential. They have positive preventive and therapeutic effects on brain neurological illnesses. Additionally, they serve a variety of biological purposes, including the prevention of diabetes, anti-inflammatory actions, cancer prevention, and anti-neurotoxicity [13].

Table 1: Plants with their phytocompounds used here

Sr.No	Plant Name	Phytocompounds
1.	*Taxillus chinensis*	1) Monotropein 2) quercetin 3-*O*-*β*-D-glucuronide 3) Procyanidin B2 4) Hyperoside 5) Astilbin 6) Pinocembrin
2.	*Carica papaya*	1) Kaempferol 2) Quercetin 3) caffeic acid 4) benzyl isothiocyanate 5) lycopene
3.	*Peltophorum africanum*	1) valerenal 2) Stearic acid 3) Luteolin 4) Ophioglonin 5) Pachypodol
4.	*Ranunculus bulbosus*	1) Rhein 2) Plumbagin 3) Pyrithione 4) Esculatin 5) Berberine
5.	*Panax notoginseng*	1) Ginsenosides 2) Sapogenin 3) Bicyclogermacrene 4) Calarene 5) Aromadendrene

METHODOLOGY

We have collected the brain images from Kaggle database. We analysed the images by python programming. This machine learning approach is used for the prediction of disease. Further, using HTS approach, we predict ligand for the disorder.

Input MRI Image

MRI brain images will be collected from various sources.

⇩

Image Processing

Cropping

⇩

Image Processing

Python programming will be used to develop the strategy for the strategy for the detection of images.

⇩

Feature Extraction

In this process, software tool will detect the brain differentiating healthy and diseases brain.

⇩

Segmentation

In the brain image segmentation, the size, Region of interest (ROI) will be detected.

⇩

Classification

This will detect the type of dementia according to image analysis.

⇩

Target Recognition

⇩

Homology Modelling

⇩

Model Evaluation

⇩

Ligand Selection

⇩

Retrieval Smiles from PubChem

⇩

ADME (Molinspiration)

⇩

Docking

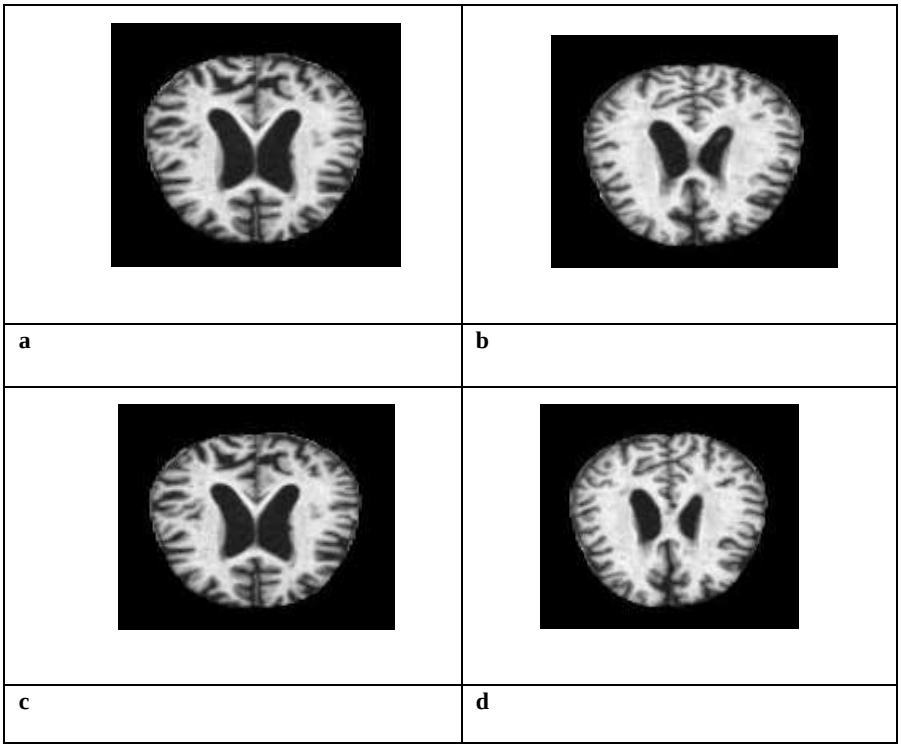
⇩

Selection as Drug Lead

Image Source:
https://www.kaggle.com/datasets/tourist55/alzheimers-dataset-4-class-of-images

Licence: Open Data Commons Open Database License (ODbL) v1.0

OpenCV python library is used for image processing (Holzer 2020).



a	**b**
c	**d**

Fig. 3: Images used in this work [retrieved from https://www.kaggle.com/code/amyjang/alzheimer-mri-modeltensorflow-2-3-data-loading/data for processing]

Code used in this work [14]

```
import numpy as np
import cv2
import sys
newimg= cv2.imread(r'/home/student/Desktop/image1.jpg') # method loads an image from the specified file.
img= cv2.resize(newimg,(340,720), fx=0.65, fy=0.55) # resize the image.
gray_scale =cv2.cvtColor(img,cv2.COLOR_BGR2GRAY) # method is used to convert an image from one color space to another.
retval,thresh=cv2.threshold(gray_scale,60,200,0) #Thresholding is a technique in OpenCV, which is the assignment of pixel values in relation to the threshold value provided.
img_contours=cv2.findContours(thresh,cv2.RETR_TREE,cv2.CHAIN_APPROX_SIMPLE)[-2] # function that helps in extracting the contours from the image.
img_contours=sorted(img_contours,key=cv2.contourArea) # returns a sorted list of the specified
iterable object. You can specify ascending or descending order.
```

```
for i in img_contours:
  if cv2.contourArea(i)>1000: # image contours is a curve joining all the continuous points (along the boundary), having same color or intensity.
    break
 mask = np.zeros(img.shape[:2],np.uint8) # the np.zeros() function returns a new array of given shape and type,with zeros.
newimg_contoyrs= cv2.drawContours(mask,[i],-50,100,-50) # to draw a contours or draw any shape provided you have its boundary points.
x,y,w,h=cv2.boundingRect(newimage_contoyrs) # function of OpenCV is used to draw an approximate rectangle around the binary image.
font= cv2.FONT_HERSHEY_SIMPLEX
cv2.putText(img,"dementia detected",(x,y-5),font,0.5,(0,0,255),1,cv2.LINE_AA) # method is used to draw a text string on any image.
cv2.rectangle(img,(x,y),(x+w,y+h),(0,600,0),2) # method is used to draw a rectangle on any image.
imgnew=cv2.bitwise_and(img,img,mask=mask) # the bitwise_and operator returns an array that corresponds to the resulting image from the merger of the given two images.
cv2.imshow("window",np.hstack([img,imgnew])) #for show image
cv2.waitKey(0) #  allows users to display a window for given milliseconds or until any key is pressed.
cv2.destroyAllWindows() # function allows users to destroy or close all windows at any time after  exiting the script.
```

Homology Modeling [15]

The receptor protein for neuro-syphilis was retrieved from genbank database. Its homologous proteins (information obtained from BLAST) from protein data bank was retrieved from protein data bank.

Homology modelling of the neuro-syphilis receptor protein was performed.

Steps –

1) Select the unknown protein (Target)
2) Retrive its amino acid sequence
3) Find its Homologous Templates
4) Target template alignment
5) Model the 3D structure of the target using the structural coordinates of the template

RESULT

With the help of MRI the image processing technique we detected the dementia. In this study we have detected the enlargement of cavity in the hippocampus region of the brain, Even the shrinkage of brain can also be seen in figures 4-7.

Fig. 4: dementia detected in Fig 3(a)

Fig. 5: dementia detected in Fig 3(b)

Fig. 6: dementia detected in Fig 3(c)

Fig. 7: dementia detected in Fig 3(d)

Template selection

Using BLAST, the homologous templates for the receptor are identified as given in Table 2.

Table 2: Receptors with their templates

Description	Accession_id	Per identity	Query coverage
NP_001100354 (TREM2 Protein)	6Y6C_A	77.30%	61%
	5UD7_A	75.00%	63%
	5EL1_A	78.07%	50%

Modeller was used to create the TREM receptor's 3D structure. The models that the modeller developed were tested using the Ramachandran Plot service. Model 5 is chosen as the best model based on Ramachandran Plot analysis because it has the most residues in the core area and the least in the outside.

Table 3: Ramachandran plot analysis of TREM3 receptor.

Statistics	#res in phi psi core	#res in Phypsi allowed	#res in phi psi generous	#res in phi psi outside	
PERI.B99990001	77.5%	15.4%	5.1%	4.7%	
PERI.B99990002	81.7%	13.3%	3.1%	1.9%	
PERI.B99990003	79.6%	14.3%	4.2%	1.9%	
PERI.B99990004	79.6%	13.7%	4.8%	1.9%	
PERI.B99990005	77.5%	18.1%	3.1%	1.2%	Selected

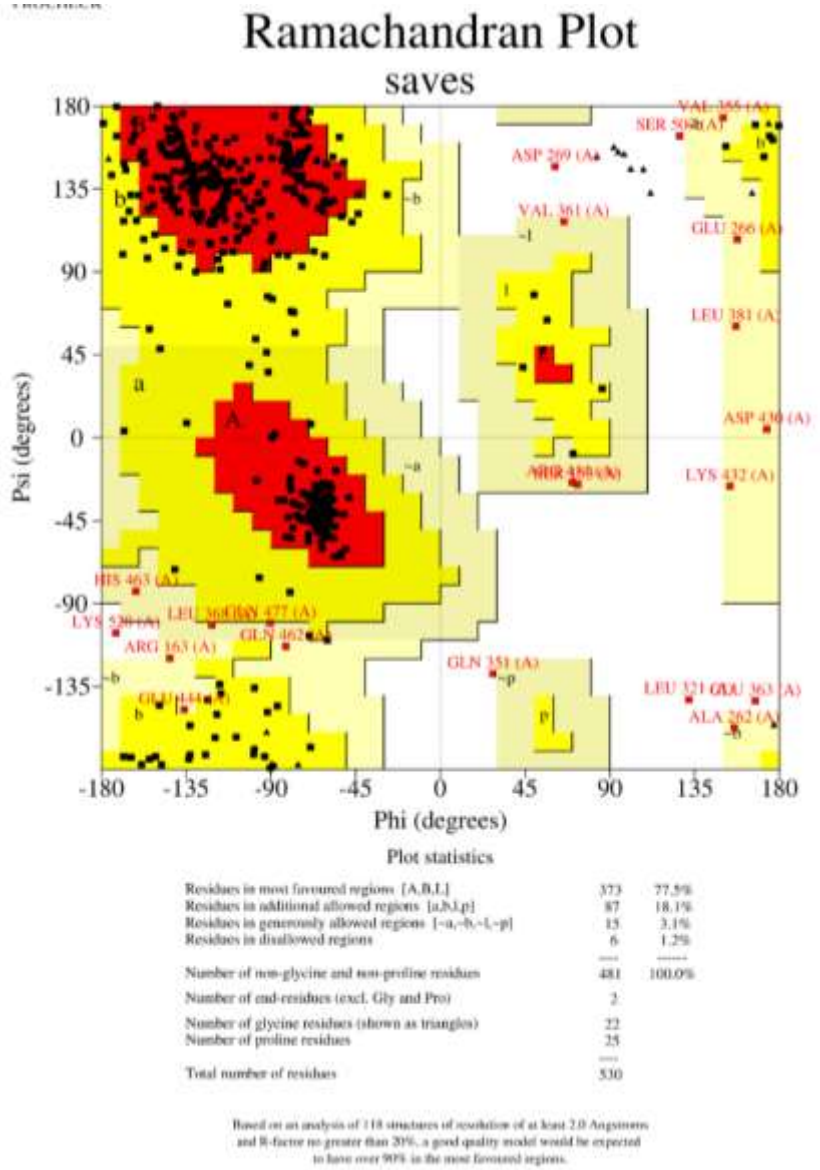


Fig. 8: Ramachandran plot of best model of TREM3 receptor

Phytocompounds' SMILES are retrived from PubChem as given in Table 4.

Table 4(a): SMILES of the phytocompounds from *Taxillus* chinensis

Scientific Name	*Taxillus* chinensis
Phytocompounds	SMILES
quercetin 3-*O*-*β*-D-glucuronide	C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O[C@H]4[C@@H]([C@H]([C@@H]([C@H](O4)C(=O)O)O)O)O)O
Monotropein	C1=C[C@@]([C@@H]2[C@H]1C(=CO[C@H]2O[C@H]3[C@@H]([C@H]([C@@H]([C@H](O3)CO)O)O)O)C(=O)O)(CO)O

Procyanidin B2	C1[C@H]([C@H](OC2=C1C(=CC(=C2[C@@H]3[C@H]([C@H](OC4=CC(=CC(=C34)O)O)C5=CC(=C(C=C5)O)O)O)O)O)C6=CC(=C(C=C6)O)O)O
Hyperoside	C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O[C@H]4[C@@H]([C@H]([C@H](O4)CO)O)O)O)O)O
Astilbin	C[C@H]1[C@@H]([C@H]([C@H]([C@@H](O1)O[C@@H]2[C@H](OC3=CC(=CC(=C3C2=O)O)O)C4=CC(=C(C=C4)O)O)O)O)O
Pinocembrin	C1[C@H](OC2=CC(=CC(=C2C1=O)O)O)C3=CC=CC=C3

Table 4(b): SMILES of the phytocompounds from *Carica papaya*

Scientific Name	*Carica papaya*
phytocompounds	SMILES
Kaempferol	C1=CC(=CC=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O[C@H]4[C@@H]([C@H]([C@@H]([C@H](O4)CO)O)O)O
quercetin	C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O)O
caffeic acid	C1=CC(=C(C=C1/C=C/C(=O)O)O)O
benzyl isothiocyanate	C1=CC=C(C=C1)CN=C=S
lycopene	CC(=CCC/C(=C/C=C/C(=C/C=C/C(=C/C=C/C=C(/C=C/C=C(/C=C/C=C(/CCC=C(C)C)\C)\C)\C)/C)/C)/C)C

Table 4(c): SMILES of the phytocompounds from *Peltophorum africanum*

Scientific Name	*Peltophorum africanum*
Phytocompounds	SMILES
valerenal	C[C@@H]1CC[C@H](C2=C(CC[C@H]12)C)/C=C(\C)/C=O
Stearic acid	CCCCCCCCCCCCCCCCCC(=O)O
luteolin	C1=CC(=C(C=C1C2=CC(=O)C3=C(C=C(C=C3O2)O)O)O)O
ophioglonin	C1C2=C(C=CC(=C2O)O)C3=C(O1)C(=O)C4=C(C=C(C=C4O3)O)O
pachypodol	COC1=CC(=C2C(=C1)OC(=C(C2=O)OC)C3=CC(=C(C=C3)O)OC)O

Table 3(d): SMILES of the phytocompounds from *Ranunculus*

Scientific Name	*Ranunculus*
phytocompounds	SMILES
Rhein	C1=CC2=C(C(=C1)O)C(=O)C3=C(C2=O)C=C(C=C3O)C(=O)O
Plumbagin	CC1=CC(=O)C2=C(C1=O)C=CC=C2O
Pyrithione	C1=CC(=S)N(C=C1)O
Esculatin	C1=CC(=O)OC2=CC(=C(C=C21)O)O
Berberine	COC1=C(C2=C[N+]3=C(C=C2C=C1)C4=CC5=C(C=C4CC3)OCO5)OC

Table 3(e): SMILES of the phytocompounds from *Panax notoginseng*

Scientific Name	*Panax notoginseng*
Phytocompounds	SMILES

Ginsenosides	CC(=CCCC(C)([C@H]1CC[C@@]2(C1CC[C@H]3[C@]2(CC[C@@H]4[C@@]3(CC[C@@H](C4(C)C)O)C)C)C)O)C
Sapogenin	C[C@]1(CC[C@@H](O1)C(C)(C)O)[C@H]2[C@H](C[C@@]3([C@@]2(CC=C4[C@H]3C[C@@H]([C@@H]5[C@@]4(CC[C@@H](C5(C)C)O)C)O)C)C)O
Bicyclogermacrene	C/C/1=C\CC/C(=C/[C@H]2[C@H](C2(C)C)CC1)/C
Calarene	CC1CCC=C2C1(C3C(C3(C)C)CC2)C
Aromadendrene	CC1CCC2C1C3C(C3(C)C)CCC2=C
Pinocembrin	C1[C@H](OC2=CC(=CC(=C2C1=O)O)O[C@H]3[C@@H]([C@H]([C@@H]([C@H](O3)CO)O)O)O)C4=CC=CC=C4

Lipinski rule of five was done using molinspiration software (Molinspiration) as given in Table 5.

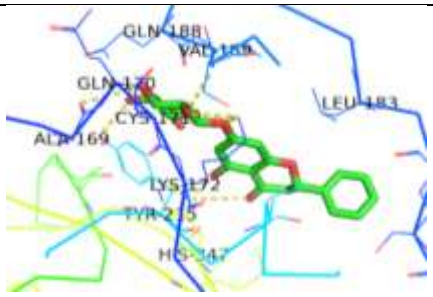
Table 5: Calculating molecular properties using In Molinspiration

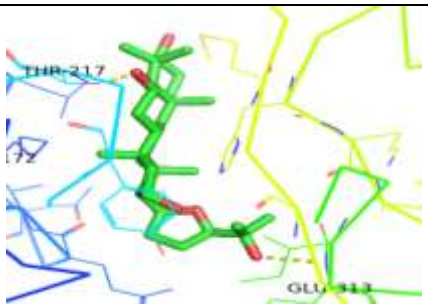
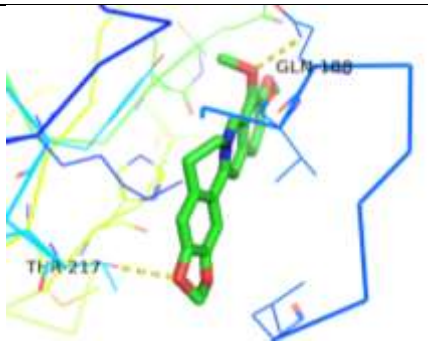
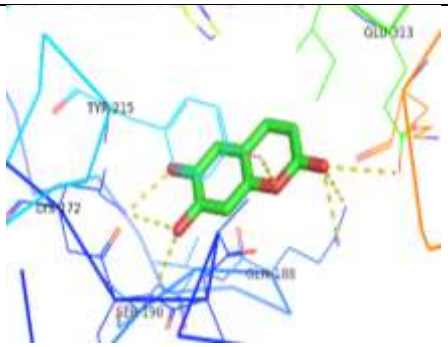
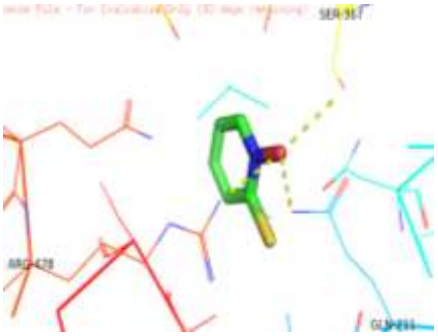
	miLogP	TPSA	natoms	MW	nON	nOHNH	nrotb	volume	nviolations
quercetin 3-*O*-*β*-D-glucuronide	-0.46	227.57	34	478.36	13	8	4	374.39	2
Monotropein	-2.93	186.37	27	390.34	11	7	5	321.73	2
Procyanidin B2	2.58	220.75	42	578.53	12	10	3	475.67	3
Hyperoside	-0.36	210.50	33	464.38	12	8	4	372.21	2
Astilbin	0.01	186.37	32	450.40	11	7	3	370.19	2
kaempferol	0.39	190.28	32	448.38	11	7	4	364.19	2
caffeic acid	0.94	77.75	13	180.16	4	3	2	154.50	2
benzyl isothiocyanate	3.00	12.36	10	149.22	1	0	2	135.62	0
lycopene	9.98	0.00	40	536.89	0	0	16	601.87	2
valerenal	4.50	17.07	16	218.34	1	0	2	232.14	0
Stearic acid	8.07	37.30	20	284.48	2	1	16	325.03	1
luteolin	1.97	111.12	21	286.24	6	4	1	232.07	0
ophioglonin	1.95	120.36	23	314.25	7	4	0	247.01	0
pachypodol	2.80	98.37	25	344.32	7	2	4	292.67	0
Rhein	3.00	111.90	21	284.22	6	3	1	225.61	0

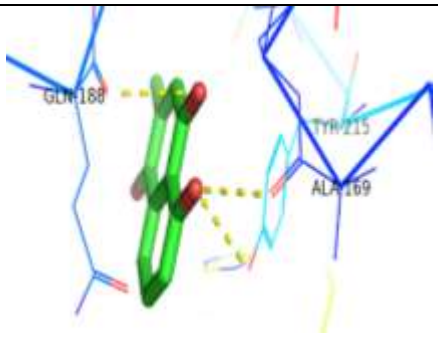
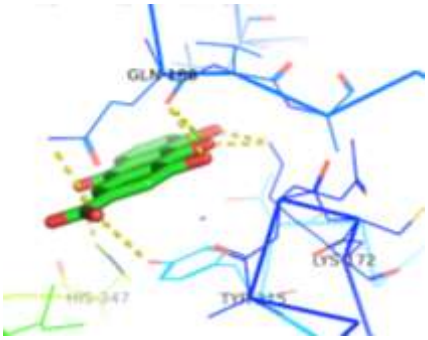
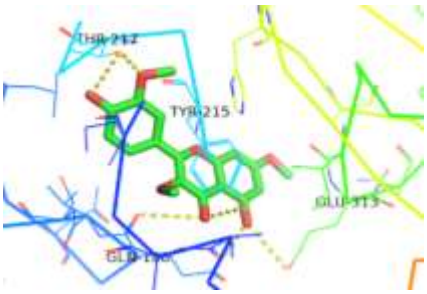
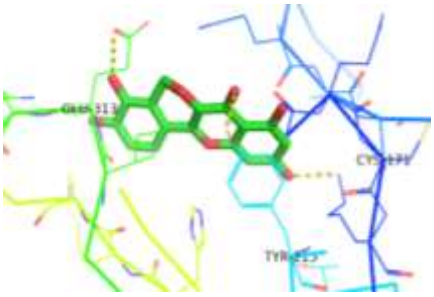
Plumbagin	1.78	54.37	14	188.18	3	1	0	163.16	0
Pyrithione	0.67	25.16	8	127.17	2	1	0	105.29	0
Esculatin	1.02	70.67	13	178.14	4	2	0	144.62	0
Berberine	0.20	40.82	25	336.37	5	0	2	296.30	0
Ginsenosides	8.02	40.46	32	444.74	2	2	4	479.88	1
Sapogenin	4.73	90.15	35	490.73	5	4	2	493.81	0
Bicyclogermacrene	5.29	0.00	15	204.36	0	0	0	229.40	1
Calarene	4.84	0.00	15	204.36	0	0	0	224.47	0
Aromadendrene	4.85	0.00	15	204.36	0	0	0	225.37	0
Pinocembrin	0.81	145.91	30	418.40	9	5	4	354.37	0

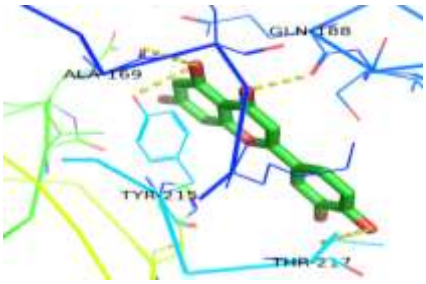
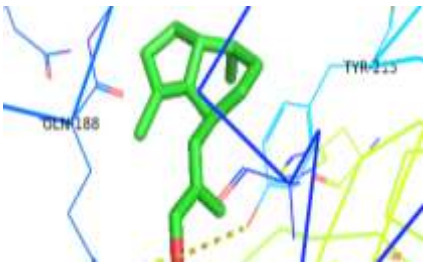
Docking was performed using hdock server [16]. Results are given in table 6.

Table 6: Docking results

	Docking image	Docking score	Interacting amino acids	No. of interactions
Model 1 Pinocembrin		-182.35 kcal/mol	LUE-187 VAL-189 GLN-188 CYS-187 GLN-170 ALA-169 CYS-171 LYS-172 TYR-215 HIS-347	1 1 1 1 1 1 1 1 1 1
Aromadendrene	No Docking	-	-	-
Calarene	No docking	-	-	-

Sapogenin (Model 1)		-157.23 kcal/mol	THR-217 GLU-313	1 1
Berberine (Model 1)		-151.60 kcal/mol	GLN -188 THR-217	1 1
Esculatin (Model-1)		-113.80 kcal/mol	GLU-313 TYR-215 LYS-172 SER-190 GLN-188	2 1 2 1 1
Pyrithione (Model-1)		-63.80 kcal/mol	SER-367 ARG-478 GLN-211	1 1 1

Plumbagin (Model-1)		-111.55 kcal/mol	TYR-215 ALA-169 GLN-188	1 1 1
Rhein (Model-1)		-156.24 kcal/mol	GLN-188 HIS-347 TYR-215 LYS-172	3 2 1 1
Pachypodol (Model-1)		-164.91 kcal/mol	THR-217 TYR-215 GLN-188 GLU-313	2 1 2 1
Ophioglonin (Model-1)		-164.43 kcal/mol	GLU-313 TYR-215 CYS-171	1 1 1

Luteolin (Model-1)		-149.76 kcal/mol	ALA-169 GLN-188 TYR-215 THR-217	1 1 1 1
Valerenal (Model-1)		-107.36 kcal/mol	GLN-188 TYR-215	1 1

DI

SCUSSION

As per previous studies the main cause for worsened neurosyphilis related dementia is the late diagnosis. Hence the main goal of this research is to identify the dementia with the help of Image Processing. In this Project we are processing the MRI images of the patients who are suffering from dementia. All datas are from other foreign countries and their climate and all other conditions are drastically different from our native conditions. Through this technique we can analyse the patient's data with all other MRI datas which will give us an exact similar information to the patients through Image processing and Machine Learning Systems and the diagnosis associated with it. This might reduce the human hours and manual efforts that go into diagnosis, yet the accuracy remains questionable.

The cause of syphilis disease is *Treponema pallidum***.**

With the improvement of technology, such as MRI scans utilised in conjunction with neuropsychological tests conducted at crucial time periods, including follow-ups, the clinician is better positioned than in the past to provide a more reliable diagnosis and prognosis. Hence, in this work we have tried to detect the disease using image processing technique. Further, the disease causal gene is taken and using homology modelling the 3d structure of the gene receptor is modelled. The model having most residues in core region and least residues in outside is selected as the best model for further docking studies.

Phytocompounds benzyl isothiocyanate, valerenal, luteolin, ophioglonin, pachypodol, Rhein, Plumbagin, Pyrithione, Esculatin, Berberine, Sapogenin, Calarene, Aromadendrene and Pinocembrin shows no violations from Lipinski's rule of five. These compounds are docked with the modelled protein.

CONCLUSION

As per the docking result it is seen that the phytocompound pinocembrin docks best with the receptor protein TREM2 with a docking score -182.35kcal/mol and at most 7 interaction hence this phytocompounds is considered as novel drug lead for the disorder neurosyphilis.

FUTURE LINE OF WORK

Since there is now no known cure for neurosyphilis, it is more crucial to reduce risk, give early intervention, and correctly and promptly identify symptoms. The literature review reveals that numerous attempts have been made to identify neurosyphilis disease using various machine learning algorithms and micro-simulation techniques; nonetheless, it remains a difficult task to uncover pertinent qualities that can identify neurosyphilis at an early stage.

The extraction and analysis of novel features that are more likely to help in the diagnosis of neurosyphilis disease will be the main emphasis of the next study. Duplicate and irrelevant features will also be removed from current feature sets to increase the precision of detection methods. We will be able to train our algorithm to distinguish between healthy persons and those with neurosyphilis by include measures like MMSE and Education. The outcome of the aforementioned technique can only detect one image at a time. The procedure can be given a database of images or an image repository as input so that it can scan through and count the number of AD, MCI, and healthy patients. Another growing area of computer science is neural networks, which are extensively used in the field of medical imaging. This offers a further option to image processing for the diagnosis of life-threatening diseases.

It is possible to do additional in vitro receptor ligand binding research to confirm (demonstrate) pinocembrin's efficacy as a treatment for neurosyphilis.

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