RESEARCH ARTICLE

In Silico Molecular Docking Analysis Of Anti-Alzheimer's Compounds From Methanolic Extraction Of *Indigofera Prostrta* And *Lantana Camara* Against Alzheimer's As A Potential Natural Lead Molecule For New Drug Design

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ABSTRACT

Alzheimer's malady (Advertisement) is neurodegenerative disarranges that have developed as among the genuine wellbeing issues of the 21st century. The drugs as of now accessible to treat Advertisement have restricted adequacy and are related with side impacts. Characteristic items are one of the foremost imperative and traditionalist sources of solutions for treating neurological issues. To assess the neuroprotective impact of MELC, MEIP in silico ponders beginning with atomic docking against Throb (PDB ID: 3LII) targets for Advertisement was conducted utilizing Auto Dock 4.1 and Molegro Virtual Docker computer program. The docking scores (kcal/mol) appeared comparatively higher strength against Advertisement related targets than right now utilized standard drugs. By and large, the potential official partiality from atomic docking, inactive thermodynamics include from MD-simulation and other multiparametric drug-ability profiles propose that MELC and MEIP may well be considered as a reasonable helpful lead for Advertisement treatment. Besides, the show comes about were unequivocally connected with the prior think about on MELC and MEIP an Alzheimer's creature show. Be that as it may, fundamental in vivo thinks about, clinical trials, bioavailability, porousness and secure dosage organization, etc. must be required to utilize MELC and MEIP as a potential sedate against Advertisement treatment, where the in silico comes about are more supportive to quicken the sedate improvement.

Keywords: Alzheimer's disease (AD), Neurological, Auto Dock 4.1, molecular docking.

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INTRODUCTION

The most common cause of dementia in people is Alzheimer's disease (Advertisement), that is. Alterations in behavior, cognitive impairments, and mistakes in the assignment of schedules and life events all act as barriers to advertising, which places a significant financial burden on the health care system [1, 2]. Dementia affects about 55 million people throughout the globe, with sixty percent of victims living in low- and middle-income countries [3]. Every three seconds, there is one thing that takes place. Each year, there are around 10 million new instances of dementia, and it is anticipated that the number of people living with dementia will reach 82 million in the year 2030 and 152 million in the year 2050 [4]. Alzheimer's illness Foundation Malaysia [5] predicts that 50,000 people in Malaysia are affected by the illness, with that number expected to increase to 100,000 by the year 2030 and 250,000 by the year 2050. Pathophysiologic abnormalities that are associated with the illness include deficiencies in acetylcholine (ACh), amyloid plaques (Aβ), tau proteins that have been overphosphorylated, and dysfunctions in the gluatamatergic system [6,7,8]. Tacrine, galantamine, donepezil, rivastigmine, and memantine are the five drugs that have been given the authorization to be used in clinical trials. It is possible to undertake pre-clinical and clinical investigations using Mellow; however, these medications have a limited viability and a large number of adverse effects [9]. It is possible to make more enticing and secure normal selections with the help of advertising dementia[10].

In spite of the constrained victory of manufactured specialists as potential multifunctional drugs against Advertisement and PD, the most constraining components such as pharmacokinetics and security issues stay challenging

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[9]. Shockingly, right now accessible solutions give only symptomatic help and don't halt neurodegeneration, making novel medicate revelations imperative. Normal items can possibly offer successful and secure pharmacodynamic characteristics in challenging neurodegenerative illnesses. Nevertheless, the multitude of biological processes and proteins implicated in the development of the disorders, the intricate nature of the affected organs (especially the brain), and their intensity remain the main obstacles to achieving significant progress in treating AD/PD. [11, 12]. Plant-derived natural products, along with their bioactive compounds, have been extensively studied in recent years for their therapeutic potential in a range of neurodegenerative diseases including Alzheimer's disease and Parkinson's disease [13, 14]. Numerous studies in epidemiological research have shown that flavonoids possess a significant neuroprotective profile among different particles [15]. An atomic docking study is a computer method used to assess the potency of a selected candidate at a critical position, specifically targeting a disease-related target. As of now, most analysts utilize progressed computational apparatuses amid 'hit' or 'lead' candidate determination [16, 17, 18]. Undoubtedly, common items or phytochemicals tend to contain multi-potent natural exercises. Hence, evaluating individual capabilities in an atypical exploratory study may be an intricate and time-consuming process. Under these conditions, atomic docking may be a more suitable method to evaluate the quality of desired characteristic agents after performing a randomised test analysis. Currently, atomic docking is regarded as a sophisticated and economical method to avoid the arbitrary and trial-and-error approach of low-intensity screening [19, 20, 21]. Nevertheless, atomic docking is a pioneering tool in contemporary drug discovery to reduce the time and resources required. This is because drug candidates for human usage cannot be proposed without extensive exploratory and theoretical considerations. Overall, atomic docking is easily understandable and has the potential to be a very effective tool in the field of pharmaceutical research. The logical evidence suggests that the predictions derived from in silico simulations are equivalent to those obtained from in vitro and in vivo experiments [22]. This work included a detailed in silico atomic docking analysis of MELC and MEIP with a protein target to enhance the advertising of a new pharmaceutical strategy.

MATERIAL AND METHODS

Plant material

Indigenous seeds of *Indigofera prostrta* and leaves of *Lantana camara* were collected from the nearby areas of Tirupati, Andhra Pradesh. Dr K. Madhava Chetty M.Sc., M.Ed., M.Phil., Ph.D., PG DPD verified the authenticity of the plants.

Maceration

After being thoroughly rinsed with water to remove any dirt or other impurities, the seeds of *Indigofera prostrta* and the leaves of *Lantana camara* were then dried in the shade. A consistent, coarse powder was obtained by grinding and sieving these dry seeds and leaves. The plant material was ground to a 1 kilogram weight, then soaked in methanol and macerated for 7 days, stirring occasionally. After 8 days, the solvent was vaporized in a rotary evaporator set at 40oC after being pressed through a muslin cloth filter. After obtaining the desired extract, it was dried in a desiccator to eliminate any remaining methanol. The *Indigofera prostrta*. (MEIP) and *Lantana camara* (MELC) dried methanolic extracts were sealed in a container and stored in a dry area for future research.

Initial Phytochemical Investigation

The presence of various primary and secondary metabolites, including carbohydrates, amino acids, proteins, lipids, tannins, phenols, flavonoids, saponins, steroids, glycosides, and resins, were confirmed by analyzing all the extracts and fractions of *Indigofera prostrta* and *Lantana camara* for these compounds using standard methods.

GC-MS investigation

The gas chromatograph-mass spectrophotometer (GC-MS) analysis was performed on a 7890A system that used a 5% phenyl methyl siloxane fused silica column (30.0m × 250µm, film thickness 0.25µm) coupled with a 5675C inert MSD equipped with a Triple-Axis detector. The column velocity flow rate was set at 1.0 ml/min using helium gas, which served as the carrier gas. The other specs for the GC-MS system are as follows: a temperature of 250°C for the ion-source, 300°C for the interface, 16.2 psi for the pressure, 1.8 mm for the out time, and a 1µl injector in split mode with a split ratio of 1:50 and an injection temperature of 300°C. Starting at 36°C for 5 minutes, the column temperature increased to 150 V at a rate of 4°C per minute. A temperature of 250°C was reached after 5 minutes of steady 20°C increments. Elution took 37 minutes in total. After comparing the average peak area of each component to the total areas, the relative percent quantity of each was determined. The system was controlled and data was acquired using MS solution software that was given by the provider.

Compounds identification

When looked at the retention indices of the components, we were able to determine their identities. Additionally, we were able to interpret the mass spectra by checking the NSIT database. The database contains more than 62,000 different patterns of compounds that are known to exist. The mass spectra of the unknown components found in the Indigofera prostrta and Lantana camara fraction were compared to the mass spectra of known components obtained from the National Institute of Standards and Technology (NISTII).

In Silico Studies MELC

Protein Processing

The RCSB Protein Data Bank (PDB) Homepage was accessed in order to obtain the PDB file that contains the three-dimensional structure of AChE (PDB ID: 3LII). Python Molecular Version was used on the protein preparations that were carried out. Establishing bonding structures was made possible by the introduction of a heavy hydrogen atom into the

Table 1: Finding of Phytochemical investigation of MEIP

S. No	*Phytochemicals name*	*MEIP*	*MELC*
1	Proteins	+	+
2	Carbohydrates	+	+
3	Alkaloids	+	+
4	Amino acids	+	+
5	Triterpenoids	+	+
6	Flavonoids	+	+
7	Phenolic compounds	+	+
8	Saponins	+	+
9	Cardiac glycosides	+	+
10	Tannins	+	+
11	Gums	-	-
12	Steroids	+	-

Where, - means negative and + means positive.

structure. Each and every ounce of water was eliminated. In the end, a force field was used in order to optimize and reduce the size of the building.

Ligand Processing

In order to convert the ligands from the SDF format found in the PubChem database (pubchem.ncbi.nlm.nih.gov) to the PDB and PDBQT formats, the program known as BIOVIA Discovery Studio Visualizer 2021 was used. After that, several modifications were made to the AutoDock software in order to take into account stereochemical variation, degree of freedom, ionization, and torsion. This was done in order to get the ligands ready for the molecular docking research.

Protein Structure for Docking

Molecular docking was accomplished via the use of docking simulations, which were carried out with the assistance of the programs AutoDock Vina and BIOVIA Discovery Studio Visualizer. In addition, the docking study was carried out by means of the command prompt method, and the Discovery Studio program was applied in order to generate the enzyme and the ligand.

RESULTS AND DISCUSSION

Flavonoids, triterpenoids, saponins, tannins,amino acids, carbohydrates and proteins, were among the phytoconstituents identified in the early phytochemical screening of the methanolic extract of *Indigofera prostrate* (MEIP).

A chromatogram of the GC-MS analysis is shown in Figure 1. The chemical components of the MEIP are summarised in Table 2, which also includes the atomic equations, molecular weights, retention durations, and percentages of area associated with each component. According to the findings of this GC-MS analysis of the methanolic fraction of Indigofera prostrta, the following bioactive compounds were found during the analysis: There are compounds such as the following included: In addition to 1-butanol, 3-methyl-formate, d-Mannose, β-Acorenol, 3-O-Methyl-d-glucose,

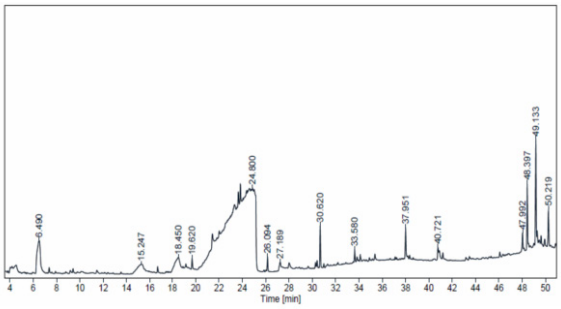


Figure 1: Methanolic extract of *Indigofera prostrta* (MEIP) GC-MS chromatograph

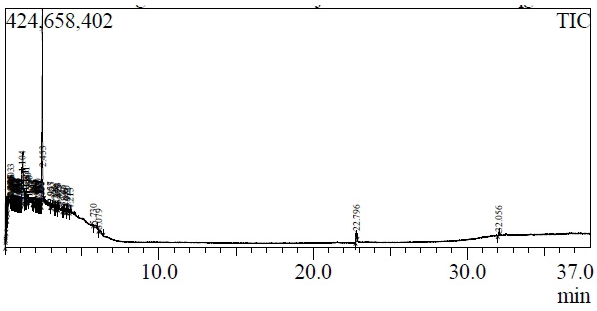


Figure 2: GC-MS chromatogram of Methanolic extract of *Lantana camara* (MELC)

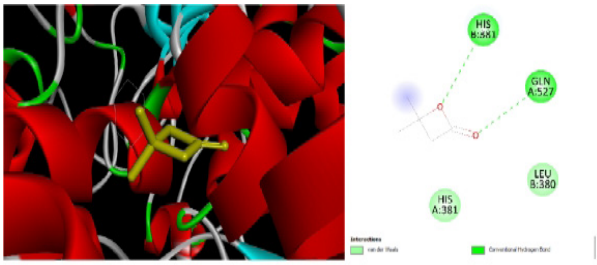


Figure 3a: 2-Oxetanone, 4, and 4-dimethyl-

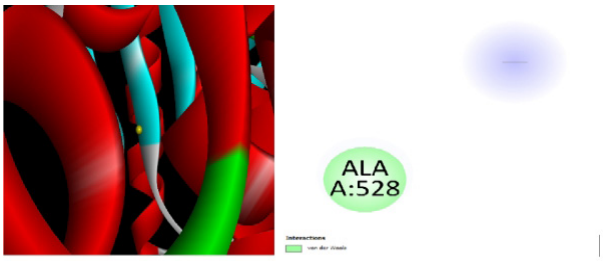


Figure 3b: Heptane, 4-ethyl-2, 2, 6, 6-tetramethyl-

Figure 3c: 1-Decene, 2-methyl-

Table 2: Bioactive components of Methanolic extract of *Indigofera prostrta* In GS-MS Analysis [MEIP]

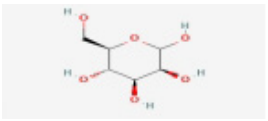
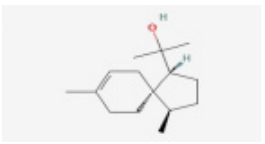
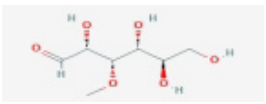
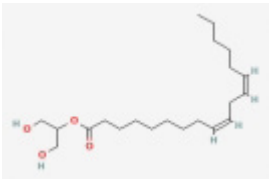
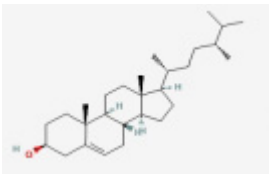
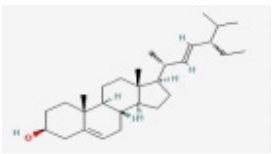
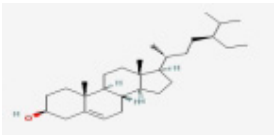
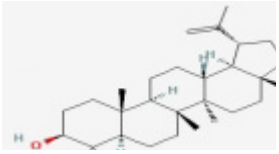
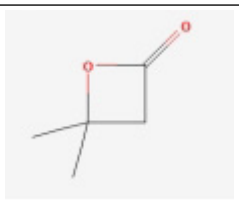
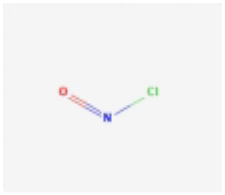
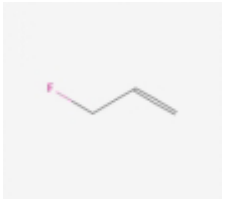
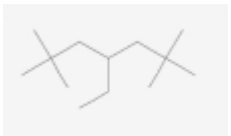
S. No	*Name of the component*	*Structure of component*	*R. Time*	*M.Wt g/mol*	*Mol. For.*	*Area%*
1	1-Butanol, 3-methyl-, formate		6.494 min	116.16	$C_6H_{12}O_2$	19.34
2	d-Mannose		15.246 min	180.156	$C_6H_{12}O_6$	8.06
3	β-Acorenol		19.621 min	222.37	$C_{15}H_2O_6$	0.59
4	3-O-Methyl-d-glucose		24.797 min	194.18	$C_7H_{14}O_6$	7.55
5	Hexadecanoic acid, methyl ester		26.091 min	270.5	$C_{17}H_{34}O_2$	1.56
6	n-Hexadecanoic acid		27.191 min	256.42	$C_{16}H_{32}O_2$	6.49
7	Phytol		rt: 30.623 min	296.5	$C_{20}H_{40}O$	4.70
8	E-8-Methyl-9-tetradecen-1-ol acetate		rt: 33.580 min	268.4	$C_{17}H_{32}O_2$	0.79
9	Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester		rt: 37.950 min	330.5	$C_{19}H_{38}O_4$	4.11
10	9,12-Octadecadienoic acid (Z,Z)-, 2-hydroxy-1-(hydroxymethyl)ethyl ester		40.719 min	354.5	$C_{21}H_{38}O_4$	5.43
11	Campesterol		47.989 min	400.7	$C_{28}H_{48}O$	1.21
12	Stigmasterol		48.395 min	412.7	$C_{29}H_{48}O$	6.42
13	γ-Sitosterol		49.133 min	414.7	$C_{29}H_{50}O$	12.59
14	Lupeol		50.214 min	426.7	$C_{30}H_{50}O$	8.35

Table 3: Bioactive compounds of Methanolic extract of *Lantana camara* in GS-MS Analysis (MELC)

S. No	*Name of the compound*	*Structure*	*Retention Time*	*Molecular Weight*	*Molecular Formula*	*% Area*
1.	2-Oxetanone, 4,4-dimethyl-		0.033	100	$C_5H_8O_2$	6.59
2.	Difluorinemonoxide		4.213	54	F_2O	0.18
3.	Nitrosyl chloride		2.957	65	ClNO	0.41
4.	Ethane, 1-chloro-1-fluoro-		0.860	82	C_2H_4ClF	0.87
5.	Carbonic chloride fluoride		0.765	82	CClFO	0.11
6.	Tetraborane (10)		1.104	54	B_4H_{10}	20.93
7.	1-Propene,3-fluoro-		1.321	60	C_3H_5F	5.22
8.	Heptane,4-ethyl-2,2,6,6-tetramethyl-		1.371	184	$C_{13}H_{28}$	2.12
9.	1-Decene,2-methyl-		1.480	154	$C_{11}H_{22}$	2.05

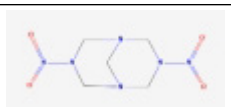
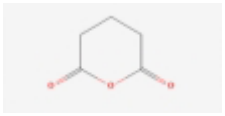
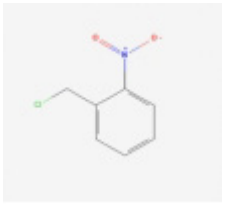
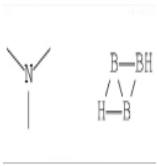
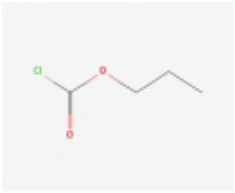
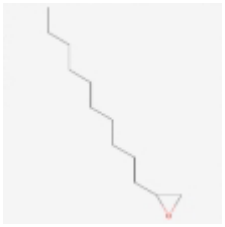
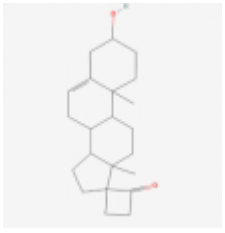
10.	N, N-Dinitro-1, 3, 5, 7-tetrazabicyclo [3, 3, 1] nonane		3.849	208	$C_5H_{10}N_6O_4$	0.26
11.	2H-Pyran-2,6(3H)-dione,dihydro-		2.224	114	$C_5H_6O_3$	0.18
12.	Benzene,1-(chloromethyl)-2-nitro-		2.453	171	$C_7H_6ClNO_2$	13.90
13.	Methanamine, N,N-dimethyl-, compd.withtriborane(7) (1:1)		2.995	99	$C_3H_{16}B_3N$	0.63
14.	2-Oxetanone, 4-methylene-		3.980	84	$C_4H_4O_2$	0.32
15.	Propane,1-chloro-		4.022	78	C_3H_7Cl	0.20
16.	Carbonochloridic acid, propyl ester		5.730	122	$C_4H_7ClO_2$	1.99
17.	Propanenitrile, 2,2-dimethyl-		6.079	83	C_5H_9N	1.64
18.	Oxirane, decyl-		22.796	184	$C_{12}H_{24}O$	2.90
19.	Spiro [androst-5-ene-17, 1'-cyclobutan]-2'-one, 3-hydroxy-, (3.beta, 17.beta.)-		32.056	328	$C_{22}H_{32}O_2$	0.88

Figure 3d: N, N-Dinitro-1, 3, 5, 7-tetrazabicyclo [3, 3, 1] nonane

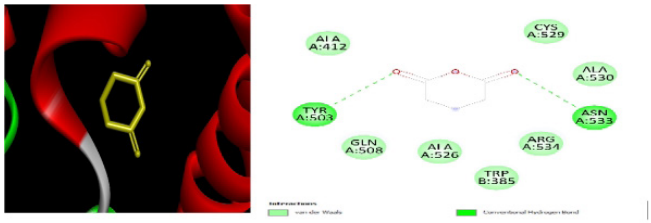


Figure 3e: 2H-Pyran-2, 6(3H)-dione, dihydro-

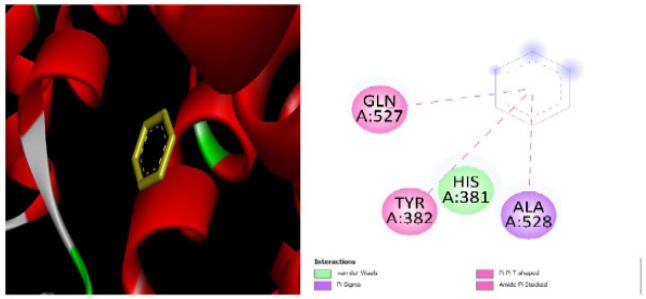


Figure 3f: Benzene, 1-(chloromethyl)-2-nitro-

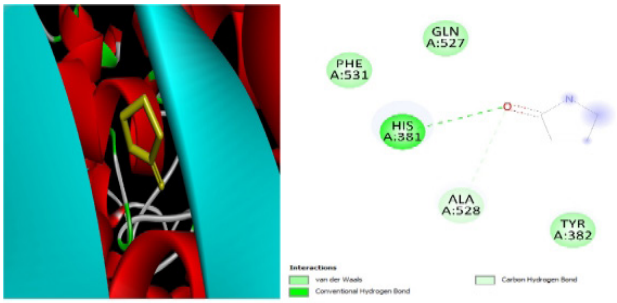


Figure 3g: piracetam
Figure 3: 2D and 3D structures of MELC

Table 4: *In silico* docking score top six compound in MELC and standard Piracetam

S. No	*Top Four compounds*	*Dock score*
	2-Oxetanone, 4,4-dimethyl-	-5.8
	Heptane, 4-ethyl-2, 2, 6, 6-tetramethyl-	-4.3
	2 H-Pyran-2, 6(3 H)-dione, dihydro-	-4.6
	1-Decene, 2-methyl-	-4.3
	Benzene, 1-(chloromethyl) -2- nitro-	-4.3
	N, N-Dinitro-1, 3, 5, 7-tetrazabicyclo [3, 3, 1] nonane	-5.4
	Piracetam	-4.4

Table 5: *In Silico* Studies MEIP

S. No	*Compound name*	*Docking score*
	1-Butanol, 3-methyl-, formate	-3.8
	d-Mannose	-6.3
	3-O-Methyl-d-glucose	-4.7
	Piracetam	-4.4
	Hexadecanoic acid, methyl ester	-4.5
	Lupeol	-8.0
	n-Hexadecanoic acid	-4.4
	Stigmasterol	-8.1
	Phytol	-4.8
	Campesterol	-7.8
	E-8-Methyl-9-tetradecen-1-ol acetate	-4.8

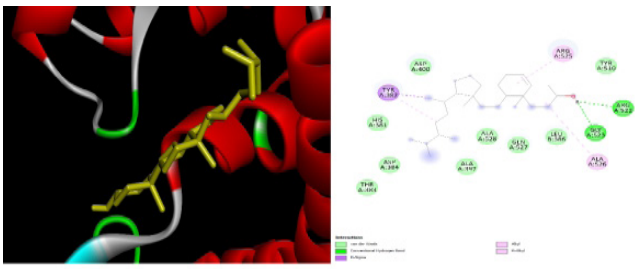


Figure 4a: Campesterol

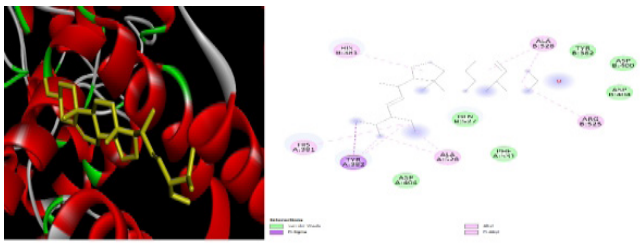


Figure 4b: Stigmasterol

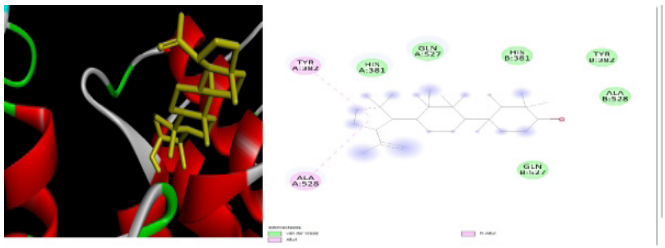


Figure 4c: Lupeol

n-Hexadecanoic acid, Phytol, E-8-Methyl-9-tetradecen-1-ol acetate, and Hexadecanoic acid with methyl ester, the following compounds are also present. Among the chemicals that belong to this category are Lupeol, Campesterol, Stigmasterol, γ-Sitosterol, and 2-hydroxy-1-(hydroxymethyl)ethyl ester.

A chromatogram of the GC-MS analysis, as illustrated in Figure 2. The chemical components are shown in Table 4, together with their Retention Time (RT), atomic equation,

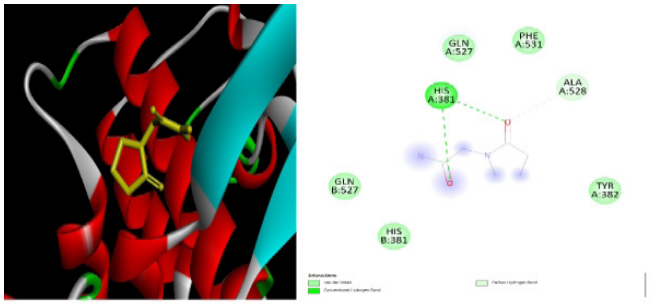


Figure 4d: Piracetam
Figure 4: 2D and 3D structures of MEIP

Molecular weight (MW), and Area (%) inside the MELC. Additionally, the atomic equation is presented. Lanata camara was extracted using methanol, and the resulting extract contained the following bioactive species: 4-ethyl-2, 2, 6, 6-tetramethyl-' N, N-dinitro-1, 3, 5, 7-tetrazabicyclo[3, 3, 1] is the chemical formula for heptane. Spiro[androst-5-ene-17,1'-cyclobutan] is a nonane chemical. Also known as:The compound -2'-one,3-hydroxy-(3.beta,17.beta...)

As part of the docking strategy, it was necessary to anticipate the compliance and introduce ligands inside a certain official area. Generally speaking, docking exams are conducted with two goals in mind: (1) exact auxiliary demonstrating, and (2) modify action prediction. There are several stages of preparation involved in docking, and each step is characterized by various degrees of difficulty. This is the conventional thinking. The initial phase in the process involves making use of docking calculations in order to position microscopic particles inside the dynamic location. These calculations are supplemented by scoring capabilities that assess the intuitive associations that already exist between particles and potential targets. This allows for the prediction of how particles would move in a natural environment. In order to study the neuroprotective effects of MELC and MEIP, we chose five human protein targets linked with advertising and four human protein targets associated with Parkinson's disease (PD) using an in silico atomic docking technique. This table provides a summary of the protein targets as well as the criteria for determination that were used inside the display assessment section. The three-dimensional (3D) gem structure of the chosen targets was obtained by using the protein data bank (PDB) with specific PDB IDs. This was done in compliance with the criteria.

CONCLUSION

Plants that are utilized for medicinal purposes may have been the source of the bioactive compounds that are used to treat a broad variety of ailments. A seed extract from *Indigofera prostrta*, which was extracted using methanol, and a leaf extract from *Lantana camara*, which was detected using GC-MS, were both subjected to in silico molecular docking research. The objective of this research was to identify the phytoconstituents of both extracts, as well as their potential interactions with Aβ and AChE, which are two essential targets in Alzheimer's disease. The outcomes of the present research provide support to the hypothesis that extracts from *Indigofera prostrta* and *Lantana camara* include phytoconstituents that have an effect on Alzheimer's disease (AD). Furthermore, in vivo experiments that make use of phytoconstituents derived from *Indigofera prostrta* and *Lantana camara* have the potential to be used in the discovery of novel leads that may be developed and enhanced into more effective Alzheimer's disease treatments. The findings of the in silico molecular docking reveal that the compounds that were screened from the methanolic seed extract of *Indigofera prostrta* and the leaf extract of *Lantana camara* potentially have the potential to be lead compounds in the battle against Alzheimer's disease. Researchers are always attempting to develop new methods to treat and manage Alzheimer's disease.

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