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In silico and *in vitro* approach of *senna alata* methanolic leaf extract as potent anti-alzheimer's

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Abstract
This research work explores the anti-alzheimer's effect of phytocompounds identified from methanolic leaf extract of *Senna alata* using GC-MS analysis and molecular docking studies. Acetylcholinesterase inhibitors improved cholinergic deficit in the brain which are beneficial in the treatment of Alzheimer's disease. In this research work we studied the AchE antagonistic effect of phytocompounds identified from *Senna alata* using an in silico approach. This work reported the phytochemical analysis of the methanolic extract of the leaves of *Senna alata*. Eight compounds were revealed through GC-MS analysis and screened using GC-MS QP2010PLUS, Shimadzu, Japan. Interpretation on mass spectrum of GC-MS was done using the database of National Institute Standard and Technology (NIST). Molecular docking of *Senna alata* on human AchE protein was determined by using Auto Dock Vina software and compared with Donepezil a known reversible acetylcholinesterase inhibitor. The interactions of Human Acetylcholinesterase-ligand conformations, including hydrogen bonds and various other bonds were analyzed using BIOVIA Discovery Studio 2016. Docking studies revealed that 9-Octadecenoic acid (2-phenyl-1,3-dioxolan-4-yl) methy lester, cis- (-7.7), Heptadecanoic acid 16- methyl acid methyl ester(7.0) existing phytochemicals from the leaves of *Senna alata* had the highest fitness score of -7.7 and -7.0 kcal/mol comparable with donepezil having -9.2 kcal/mol and hence could be a potent antialzheimer's drugs. *Senna alata* leaf extract and its compounds 9-Octadecenoic acid (2-phenyl-1, 3-dioxolan-4-yl) methylester, cis-, Heptadecanoic acid 16- methyl acid methyl ester have significant antialzheimer's activity against AchE. The molecular docking interaction of an in-silico data demonstrated that 9-Octadecenoic acid (2-phenyl-1,3-dioxolan-4-yl) methylester, Heptadecanoic acid 16- methyl acid methyl ester has more specificity towards the AchE binding site and could be a potent antialzheimer's compound.

Keywords: *Senna alata*, GC-MS, docking studies, acetylcholinesterase

Introduction
Alzheimer disease is characterized by the accumulation of Aβ plaques around the neurons extracellularly and formation of neurofibrillary tangles by hyperphosphorylation of Tau proteins intracellularly that results decrease in the level of Ach neurotransmitter [1]. In brain cholinergic neurons synthesise acetylcholine a neurotransmitter involved in the signal transmission and delivery of messages in the brain [2, 3]. It plays an important role in learning and memory [4, 5]. Deposition of plaques and neurofibrillary tangle in the brain which leads to degradation of the cholinergic neurons in the hippocampal and cortical part of the brain and decrease in the level of acetylcholine [6, 10]. Decrease acetylcholine level is responsible for unregulated signal transmission of the cholinergic pathway which is accompanied by AD.
Hence the AchE inhibitors are beneficial in the treatment of Alzheimer's disease. Currently two pharmacotherapy's are approved by Food and Drug Administration (FDA) i.e. Acetyl cholinesterase inhibitor like Tacrine, Donepezil, Rivastigmine, Galantamine and N-methyl D-aspartate, glutamate antagonist (NMDA) - Memantine.
Senna alata leaves extract commonly used to treat ringworm, fungicidal and has an antibacterial, laxative, anti-inflammatory, anti-tumor and diuretic property. Clinical trials are not conducted to till date. Need to screen important folk uses, and to find new bioactive molecules with pharmacological purpose based on the demand.

Materials and Methods
Selection of the Plant
Drug discovery from medicinal plants has evolved to include numerous fields of inquiry and various methods of analysis. The process typically begins with a botanist, ethno botanist, ethno pharmacologist, or plant ecologist who identifies the plant of interest. Collection may involve species with known biological activity for which active compounds have not been isolated or may involve taxa collected randomly for a large screening program. On the basis of intensive literature survey; *Senna alata*, leaves were selected for present study.

Collection and Authentication of Plant Material
The plants *Senna alata* leaves had been collected from ABS botanical garden, Salem, Tamil Nadu, India. The plant was identified and authenticated by the botanist Mr. A. Balasubramanian (consultant – central siddha research) Executive Director ABS botanical, Salem, Tamil Nadu.

Extraction of Plant Material
The fresh leaves of *Senna alata*, *a*re collected and dried under shade, sliced into small pieces and ground into powder with mechanical grinder and the powder was sieved by Sieve no.30 and preserved in a container.

Solvents for Extraction
Petroleum ether (60-80°C)

Chloroform
Methanol

Extraction procedure
The dried powder of leaves of *Senna alata* was defatted with petroleum ether in Soxhlet apparatus by hot percolation. The defatted powder material (marc) thus obtained was further extracted with Chloroform and methanol. The solvent was removed by distillation under reduced pressure and evaporation. The resulting semisolid mass was vaccum dried by using rotary flash evaporator.

Preliminary Phytochemical Studies [11-14]
The extract was subjected to preliminary phytochemical investigations to identify various phytoconstituents present in the leaves of *Senna alata.*

Identification of Phytochemical Constituents using Gas Chromatography [15].
GC-MS analysis was carried out by GC-MS QP2010PLUS, Shimadzu, Japan coupled with mass spectrometry as detector. The temperature was adjusted to -30°C to 280/300°C, the HP-5MS column with dimensions 30 m X 0.32 mm X0.25 µm was used for analysis. The oven temperature was adjusted to 35°C and hold time 5 min and, ramp 10°C/min up to 220°C. Column flow is 1.2 ml. The inlet temperature was kept at 250°C and the source temperature of 230°C and MS Quard temperature of 150°C.

Molecular docking studies [16].
Human Acetyl cholinesterase binding mode and interaction with individual Phytoconstituent was performed using AutoDock Vina software. Possible conformations and orientations for the ligand at the binding site were obtained by Molecular docking. The PyRx software used to load the protein, creating a PDBQT file which contains a protein structure with hydrogens in all polar residues. All ligand bonds were set to be rotatable. The protein-fixed ligand-flexible docking calculations were done using the Lamarckian Genetic Algorithm (LGA) method. The docking site on protein target was defined by establishing a grid box with the dimensions of X: 38.0729 Y: 33.3208 Z: 25.0000 Å, with a grid spacing of 0.375 Å, centered on X: 20.2892 Y: 10.3219 Z: 32.3218 Å. The lowest docked energy was chosen as best conformation, after the docking search was completed. Eight runs with Auto Dock Vina were performed in all cases per each ligand structure, and for each run the best pose was saved. The best poses average affinity was taken as the final affinity value. The interactions of Human Acetylcholinesterase-ligand conformations, including hydrogen bonds and various other bonds were analyzed using BIOVIA Discovery Studio 2016.

Preparation of protein
The water molecules, cofactors, and other ligands were removed from Crystal Structure of Recombinant Human Acetylcholinesterase in complex with Donepezil (PDB ID 4EY7) through Molegro molecular viewer. Then they were used for molecular docking studies

Preparation of ligands
The crystal 3D structures of the active compounds were retrieved from PubChem database. Energy minimization was done using Open babel version 2.4.1

***In vitro* study ($A\beta_{1-42}$ intoxicated SH-SY5Y cell lines model)**

Cell viability assessment – MTT assay [17]
SH-SY5Y human neuroblastoma cell lines were obtained from National Centre for Cell Science (NCCS), Pune, India and maintained in Minimum Essential Medium (MEM) as per the standard protocol supplemented with 10% fetal bovine serum (FBS), streptomycin (250µg/ml), gentamycin (400µg/ml), amphotericin (3µg/ml), and penicillin (250units/ml) in a carbon dioxide incubator at 5% CO_2. The viability of neuron in terms of mitochondrial metabolic function was evaluated by MTT [(3-[4, 5-dimethylthiazol-2-yl]-2, 5 diphenyl tetrazolium bromide)] assay based on the principle involving reduction of MTT to formazan. To assess the protective effect, the SH-SY5Y cells were incubated with $A\beta_{1-42}$ (10µM) for 24hrs and then post-treatment were made with methanolic leaf extracts of *Senna alata* using its IC_{50} value. Then SH-SY5Y cells were washed with phosphate-buffered saline (PBS) and incubated with MTT (5mg/ml) in PBS for 3 hours at 37°C in 5% CO2. After further washing, the formazan crystals were dissolved with isopropanol and the absorbance was measured at 570nm. The percentage of viability of SH-SY5Y cells were calculated by the standard formula (Kaja *et al*. 2011).

$A\beta_{1-42}$ intoxication and extracts treatment
The SH-SY5Y cell lines were maintained in Minimum Essential Medium (MEM) as per the standard protocol. 5000-10000 cells/well were seeded in 96 well plates and the viability was tested using trypan blue dye and 95% of viability was confirmed with help of haemocytometer. The cells were then incubated with $A\beta_{1-42}$ (10µM) for 24hrs. Then post-treatment with methanolic leaf extracts of *Senna alata* using IC_{50} values were made. After 24 hours of treatment with respective extracts the following evaluations were performed.

Cell morphological observation
The phase contrast microscopy (Motic) was used to observe morphological changes in the SH-SY5Y cell lines.

Preparation of cell lysates
After study period, the medium was aspirated and cells were washed with the ice cold phosphate buffer saline, scraped, and were centrifuged at 5000 rpm for 5 min at 4 °C. The cell pellets were resuspended in 2000 µl of lysis buffer (10mM Tris - HCl, pH 7.5, 50mM NaCl, 5mM EDTA, 1% Triton X-100, 100µM Na3VO4, 50mM NaF, 1mM PMSF, 10µg/ml aprotinin 10µg/ml and leupeptin,) and incubated on ice for 30min. The cell lysates were obtained by centrifugation at 12000 rpm for 20 min at 4 °C.Then obtained cell lysates were stored at -20 °C until use.

Lipid peroxidation (LPO) assay [18]
Lipid peroxidation was evaluated in cell lysates by measuring the malondiaaldehyde content according to the TBA test described by ohkawa *et al*., (1979) with slight modification. 0.8 ml saline, 0.5 ml of BHT and 3.5 ml TBA reagent (0.8%) were added to 0.2 ml of the cell lysate, and incubated at 60 ^{0}C. After cooling, the solution was centrifuged at 2000 rpm for 10 minutes. The absorbance of the supernatant was measured at 532 nm using spectrophotometer against the blank (Ohkawa *et al*., 1979).

Nitric Oxide (NO) assay [19]

This assay was done by taking 0.2 ml of medium with 1.8 ml of saline and 0.4 ml of 35% sulphosalicylic acid (SSA) for protein precipitation. And the precipitate was removed by centrifugation at 4000 rpm for 10 min. To 1 ml of aliquot of supernatant, 2 ml Griess reagent (1g of sulphanilamide dissolved in small volume of water, 2 ml of orthophosphoric acid and 100 mg of naphthyl ethyldiamine were added and the final volume was made upto 100 ml with distilled water) was added and the mixture was allowed to stand for 20 min under dark conditions. The colour intensity of the chromogen was read at 540 nm. Standard calibration curve was plotted using sodium nitrite in the concentration range 200- 1000ng (Green *et al*., 1982).

Reduced glutathione (GSH) [20]

GSH content was determined by following the method of Jollow *et al*. (1974). To 0.25ml of cell lysate an equal volume of ice-cold 5% TCA was added. The precipitate was removed by centrifugation at 4000 rpm for 10 mins. To 1ml aliquot of supernatant, 0.25ml of 0.2M phosphate buffer (pH 8.0) and 0.5ml of DTNB (0.6mM in 0.2M phosphate buffer, pH 8.0) were added and mixed well. The absorbance was measured at 412nm using spectrophotometer (UV, Shimadzu, Japan) (Kakkar *et al*., 1984)

Superoxide dismutase (SOD) [21]

To 0.05ml of cell lysate, 0.3ml of sodium pyrophosphate buffer (0.025M, pH 8.3) was added. To this mixture, 0.025ml and 0.075ml of PMS (186µM) and NBT (300µM in buffer, pH 8.3) were added. The reaction was initiated by the instillation of 0.075ml of NADH. The mixture was then incubated at temperature of 30°C for a period of 90 seconds. To this 0.25 ml of glacial acetic acid was added in-order to arrest the ongoing reaction. N-butanol (2ml) was shaken vigorously along with the reaction mixture and the mixture was centrifuged at 4000 rpm for 1 min. The colorimetric analysis with n-butanol (1.5ml) serving as blank (Beers and Sizer, 1952) was carried out at 560nm using spectrophotometer.

Catalase (CAT) [22]

A small quantity of cell lysate (100µl) or sucrose (0.32M) was subjected to incubation with potassium phosphate buffer (2.25ml) 65 mM at pH 7.8 for 30 min at 25°C. The reaction was initiated by the addition of hydrogen peroxide (7.5mM; 650µl). The absorbance change was recorded for a period of 2 to 3 min at 240nm (UV, Shimadzu, Japan) (Jollow *et al*., 1974).

Protein estimation [23]

Protein content in the cell lysate was estimated as described by Lowry *et al*., 1951 to quantify the above parameters per mg protein.

Measurement of IL-1β & TNF-α (Pro-inflammatory cytokines) by ELISA [24]

The levels of IL-1β and TNF-α were assessed in cell lysates by using respective ELISA kits (Invitrogen, R&D systems & Alpha diagnostics, USA) as per the manufacturer's protocol. Briefly, 150µl distilled water was added to the standard and blank wells for standard calibration and 100 µl distilled water and 50 µl of each supernatant were added in duplicate into the wells. After incubation for 3 hours at room temperature, the wells were emptied and washed three times with 150 µl of wash buffer. TMB substrate (100 µl) was added to each well and incubated for 15 min at room temperature, followed by addition of 100µl stop – solution to all wells including blank wells. The absorbance was determined at 410 nm using above mentioned ELISA reader (Roeske-Nielsen *et al*. 2004).

Results

The preliminary phytochemical studies of methanolic extract of leaves of *Senna alata* showed the presence of alkaloids, flavonoids, carbohydrates, protein, terpenoids, tannins, anthraquinone and cardiac glycosides. The results are shown in Table 1.

Table 1: Phytochemical constituents of MESA

Phytochemical constituents	Methanol extract
Alkaloids	+
Flavonoids	+
Carbohydrates	+
Protein	+
Terpenoids	+
Tannins	+
Saponins	-
Anthraquinone	+
Phlobatannin	-
Cardiac glycosides	+
Fatty acids	+

GC-MS analysis of MESA

The crude methanol extract of leaves of *Senna alata* were injected for screening of total active compounds by using GC-MS analyser. About 8 compounds were identified from the methanolic leaves extract of *Senna alata.* The retention for bioactive compounds of leaves extract ranged from 11.04 to 39.39. The compound identified from the methanolic extract of *Senna alata* using full mass spectrometry showed the presence of 4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-, 1-Butanol3-methyl-formate, Methyltetradecanoate, 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, Pentadecanoic acid 14-methyl- methyl ester, 9-Octadecenoic acid, (2-phenyl-1,3-dioxolan-4-yl) methylester, Heptadecanoic acid, 16-methyl-, methyl ester, Heptadecanoic acid, 16-methyl-, methyl ester, Myo-Inositol, 4C-methyl. Mass spectrum of a few compounds like Heptadecanoic 16 methyl acid methyl ester, 9-Octadecenoic acid (2-phenyl-1, 3-dioxolan-4-yl) methylester, Myo-inositol 4-C methyl were discussed in the present study.

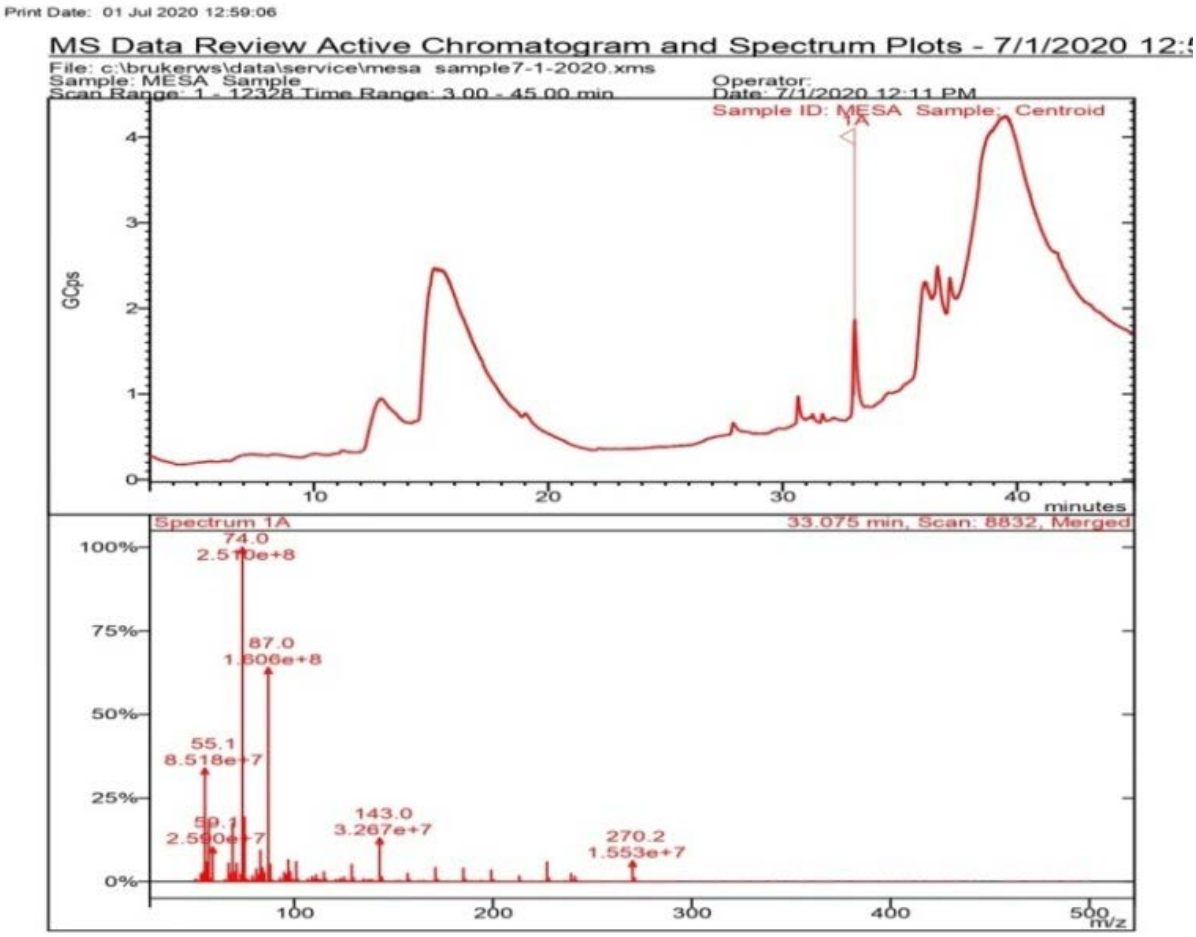

Fig 1

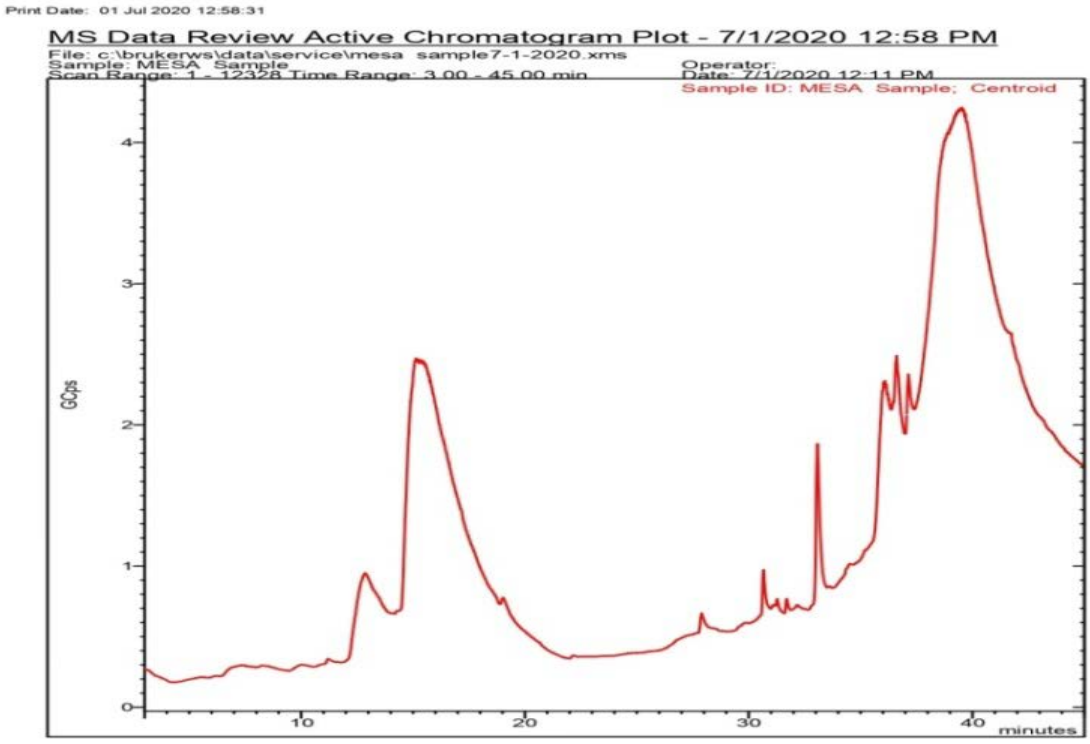

Fig 2

Molecular docking Studies

Structure based drug design

From PDB acetylcholinesterase enzyme (PDB ID 4EY7) was downloaded, it was prepared by removing chain B. Water molecule present in both the chain are removed. Energy minimization was done. Molecules drawn using chemsketch were converted to mol format and ligprep was created.

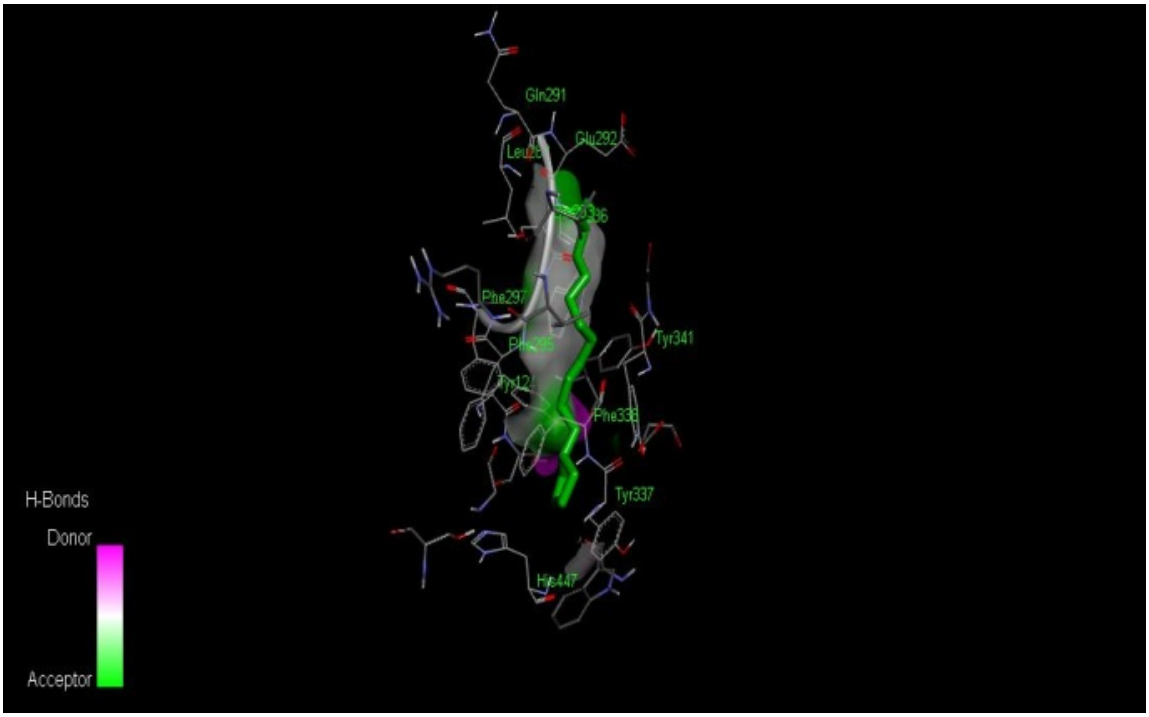

Fig 3

Compound BV1 posses their excellent interactions over the enzyme such as conventional hydrogen bond interactions in SER B: 296, pi-alkyl interactions in TYR B: 337, PHE B:338 and vanderwaals interactions in GLN B: 291, HIS B 447, PHE B 297, TYR B 341, 124, PHE B:295, VAL B: 294, TRP B: 286, LEU B: 289.

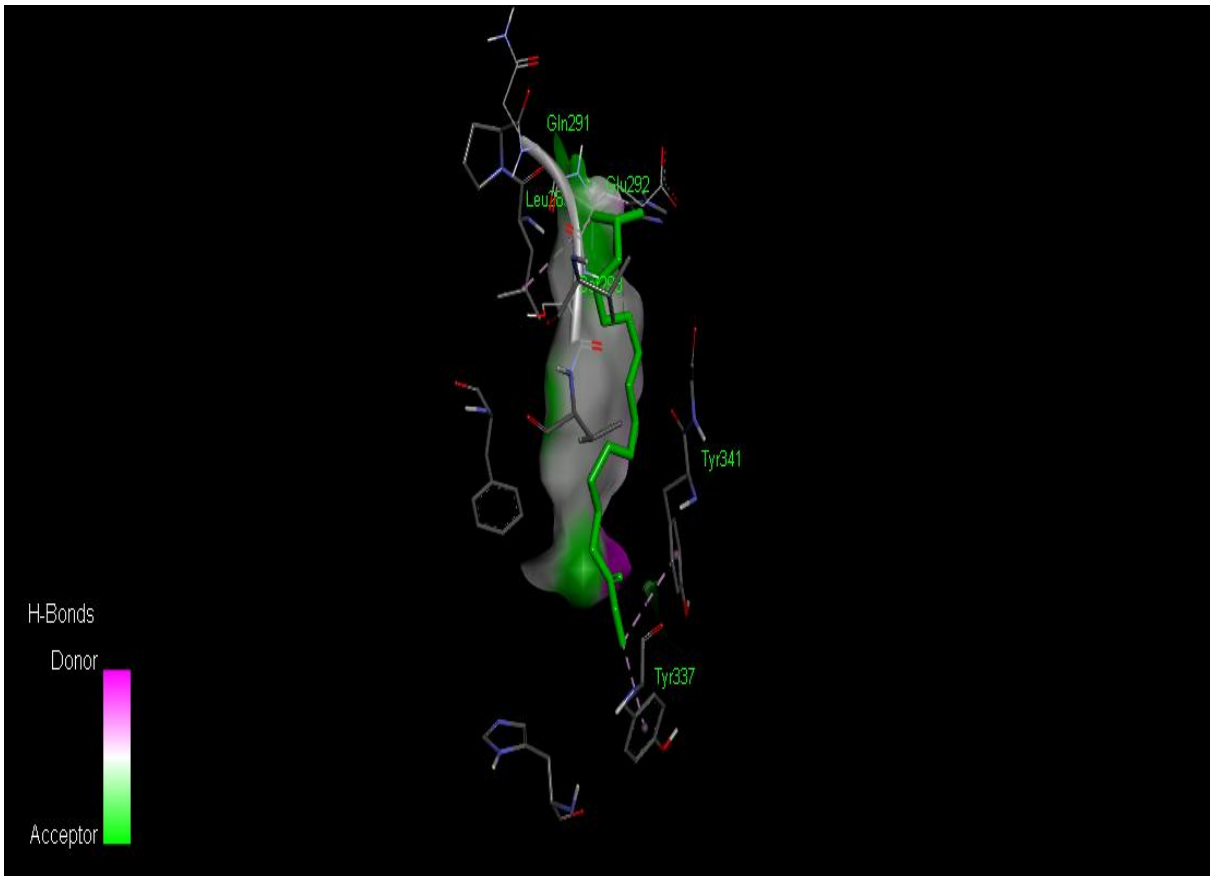

Fig 4

Docking analysis of compound BV2 posses their pi-alkyl interactions over the enzyme TYR B: 341, LEU B: 289, and alkyl interactions in TYR B: 337 and vanderwaals interactions in PHEb: 297, VAL B: 294, SER B: 293, GLU B: 292, GLN B: 291.

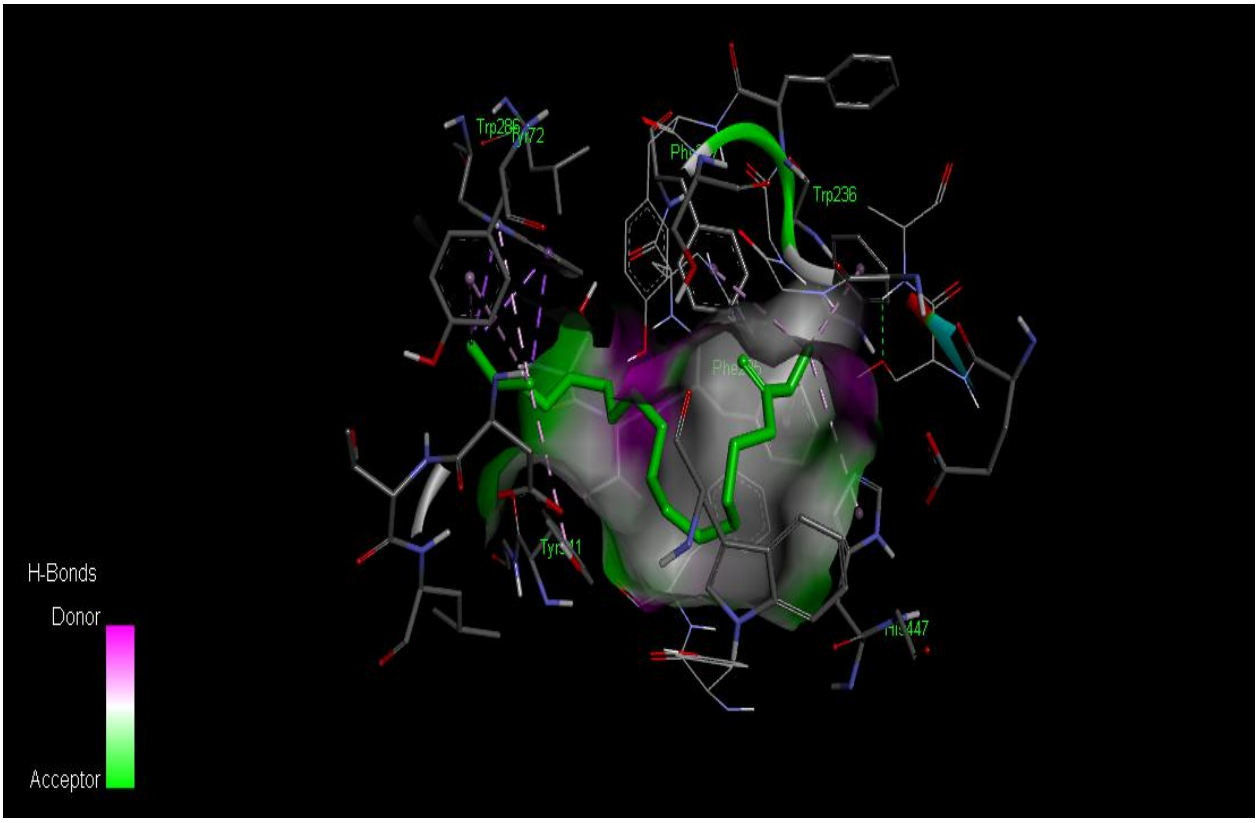

Fig 5

Compound BV3 shows their pi-sigma interactions over the enzyme TRP A: 286, pi-alkyl interactions in PHE A: 297, 295, TRIP A: 236, HIS A 447, TYR A: 341, 72, and has a vanderwaals interactions in AGR A: 296, VAL A: 294, TYR A: 124, GLY A: 121, 122. PHE A: 338, ALA A: 204, SER A: 203, TYR A: 337.

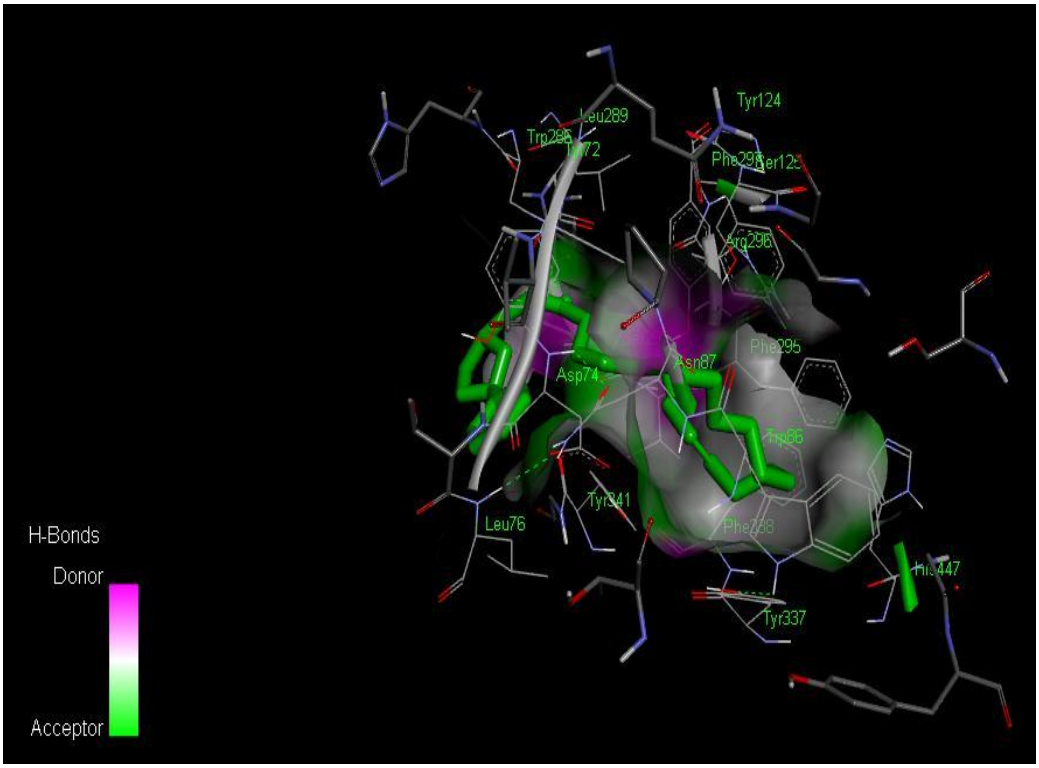

Fig 6

Compound BV4 Posses their conventional hydrogen bond interactions over the enzyme SER A: 293, pi-alkyl with LEU A: 76 and also has a vanderwaals interactions in GLU A: 292, ASN A: 87, TYR A: 72, ASP A: 74, LEU A 289, SER A: 125, TRP A 86, TYR A: 337, TYAR A 341, VAL A 294, ARG A: 296, PHE A: 295, 297, 338.

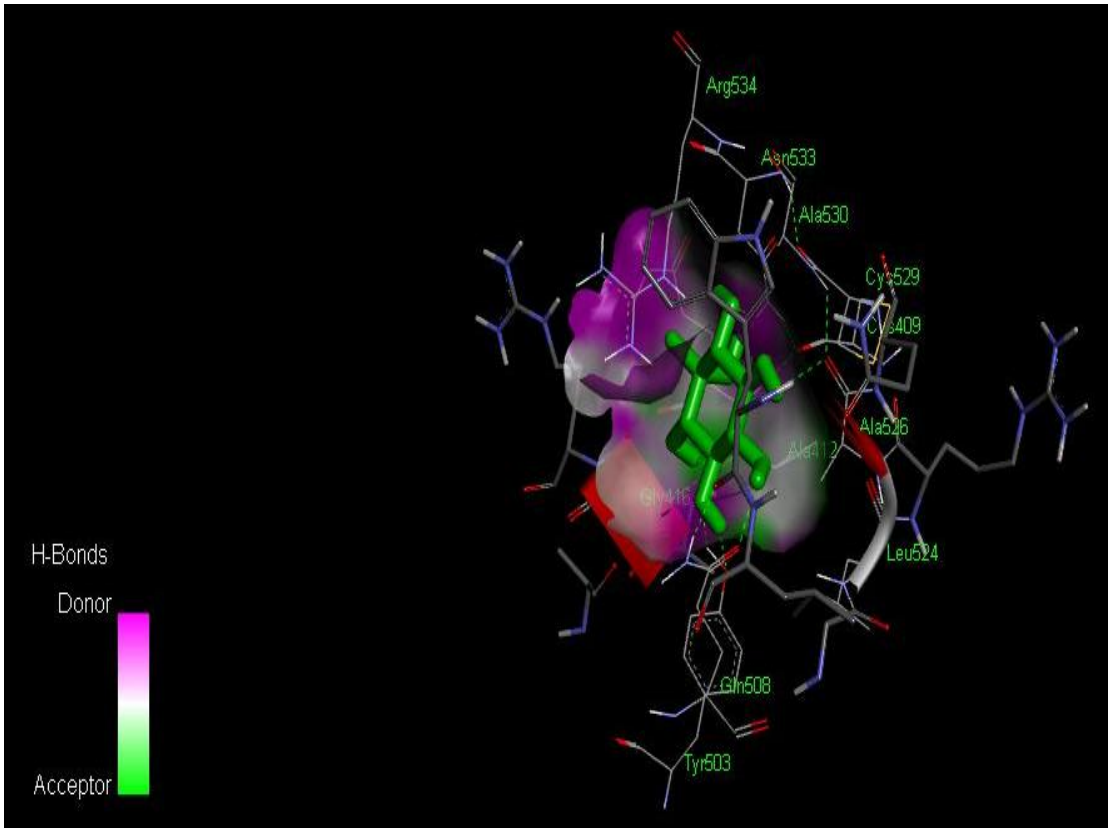

Fig 7

Compound BV5 posses their best covalent hydrogen bond interactions over the enzyme ALA B: 412, GLN B: 508, ALA B 526, and have vanderwaals interactions in CYS B: 409, 529, ARG B: 534, ALA B: 530,505, TRB A: 385, GLY B: 523, 416, LEU B: 524, TYR B: 503, GLN B: 413.

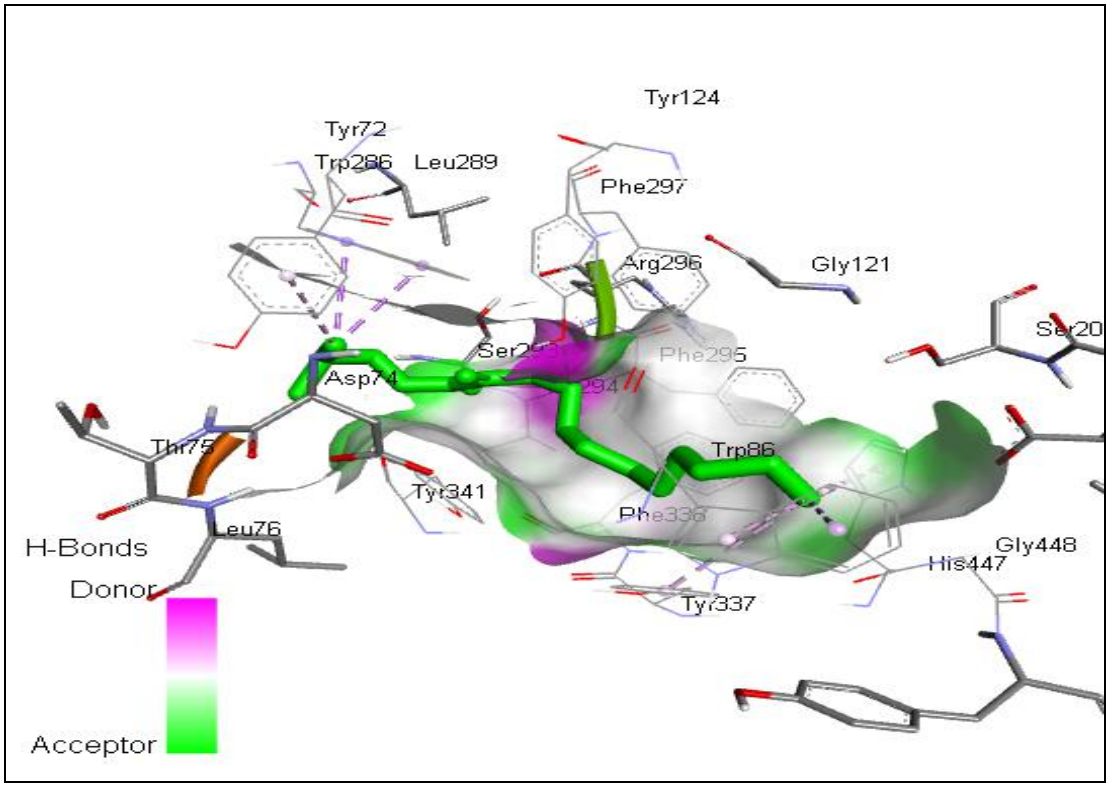

Fig 8

Compound BV6 Posses their Carbon hydrogen bond interactions over the enzyme TYR A: 124, 341and pi-sigma interactions with TRP A 286, 86, pi-alkyl interactions in TYR A: 337, 72, HIS A: 447 and vanderwaals interactions with VAL A: 294, PHE A: 295,297,338.

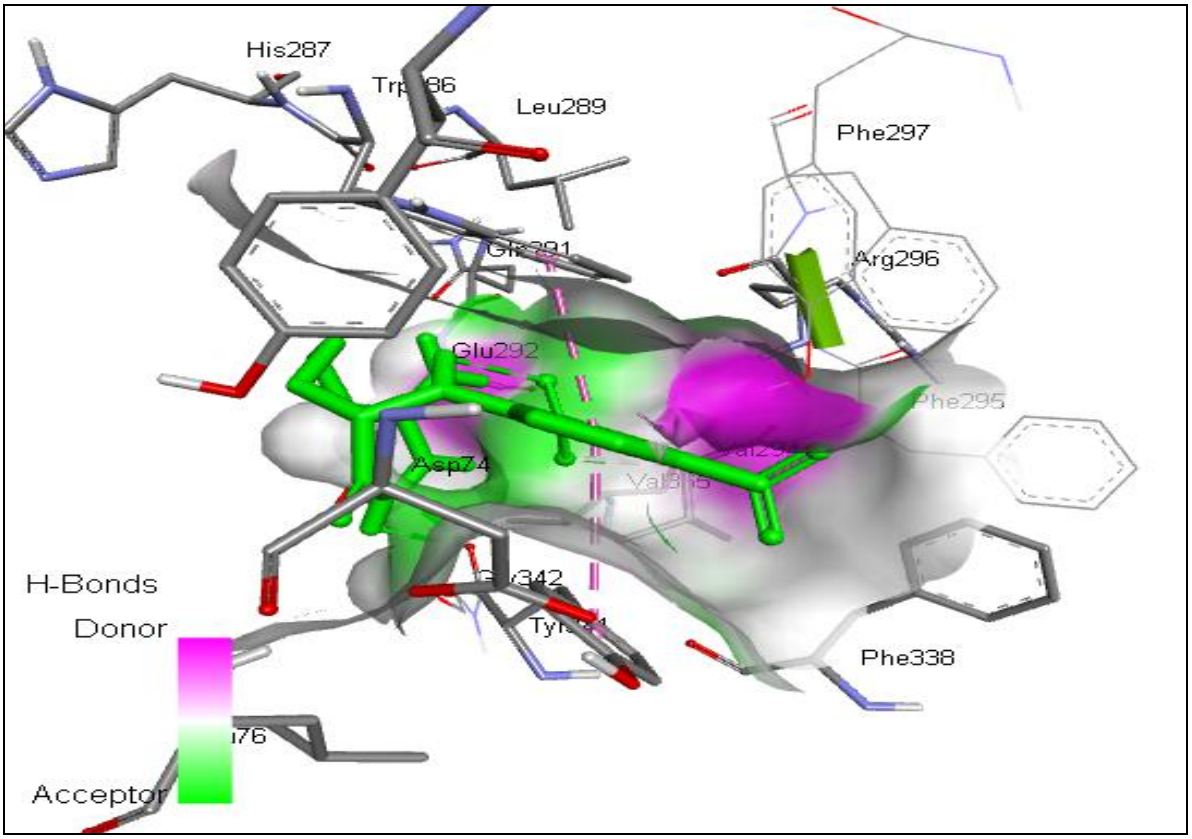

Fig 9

Compound BV 7 Posses conventional hydrogen bond interactions over the enzyme TYR A: 341, and pi-pi stacked interactions with TRP A: 286, TYR A: 341, carbon hydrogen bond interaction in VAL A: 294. It has a vanderwaals interaction in GLY A 342, PHE A: 295, 338,297, TYR A 124, 72, LEU A 76, 289, GLU A 292.

Table 2: Binding affinity of the compounds with Donepezil (PDB ID 4EY7)

Ligand	Target Protein	Binding Affinity	RMSD
BV1	Recombinant Human Acetylcholinesterase in complex with Donepezil (PDB ID 4EY7)	-6.9	0
BV2		-5.6	0
BV3		-7.0	3.232
BV4		-7.7	0
BV5		-6.7	0
BV6		-6.3	0
BV7		-6.5	0
Standard(Donepezil)		-9.2	0

In Vitro cytotoxicity MTT assay of methanolic leaf extracts of *Senna alata* in SH-SY5Y cell lines

Table 3: MTT assay results

Sl No.	Sample Description	SHSY5Y IC_{50} µg/ml
1	Methanolic leaf extracts of *Senna alata*	69.77825

Inhibition concentration of *Senna alata* was found to be 69.77 µg/ml.

Cell viability assessment – MTT assay [in presence of amyloid-beta$_{1-42}$ (Aβ$_{1-42}$)]

Table 4

S. No	Groups	% viability of cells
1	Control	99.87 ± 0.143
2	Aß$_{1-42}$ (10µM)	11.22 ± 0.473***
3	met-L-SA	59.17 ± 4.671$^{###}$

Table 4: Effect of methanolic leaf extracts of *Senna alata* (met-L-SA) on cell viability level in Aβ1-42 intoxicated SH-SY5Y cell lines. Statistical significance was determined by one way ANOVA followed by Tukey's multiple comparison tests using Graph pad prism Version 6.0. Values are represented as Mean ± SEM, Superscript *** denotes $p<0.001$ vs control, ### denotes $p<0.001$ vs Aβ1-42 groups respectively, (Aβ: Amyloid beta).

Anti-oxidant evaluation – Spectroscopy methods

Table 5

S.NO	Groups	LPO nmoles/ml	NO nmoles/ml	Cellular GSH (µm/mg protein)	SOD (U/mg protein)	CAT (U/mg protein)
1	Control	12.93± 1.74	24.20± 2.10	85.55±4.33	25.17± 2.28	0.907±0.090
2	$A\beta_{1-42}$	95.30± 3.38***	147.63± 2.39***	11.23± 1.44***	3.54± 0.87***	0.172±0.035***
3	Met-L-SA	62.15± 1.72###	78.94± 3.76###	59.92± 2.96###	12.87± 0.85###	0.518±0.029###

Table 5: Effect of methanolic leaf extracts of *Senna alata* (met-L-SA) on LPO, NO, GSH, SOD, CAT level in Aβ1-42 intoxicated SH-SY5Y cell lines. Statistical significance was determined by one way ANOVA followed by Tukey's multiple comparison tests using Graph pad prism Version 6.0. Values are represented as Mean ± SEM, Superscript *** denotes p<0.001 vs control, ### denotes p<0.001 vs Aβ1-42 groups respectively, (Aβ: Amyloid beta).

Antiinflammatory Assessments

Table 6

S.NO	GROUPS	IL-1β (pg/ml)	TNF-α (pg/ml)1
1	Control	105.23± 1.22	133.71± 5.37
2	$A\beta_{1-42}$	889.87± 17.89***	977.84± 36.52***
3	Met-L-SA	623.87± 32.65###	675.24± 18.14###

Table 6: Effect of methanolic leaf extracts of *Senna alata* (met-L-SA) IL-1β and TNF-α level in $A\beta_{1-42}$ intoxicated SH-SY5Y cell lines. Statistical significance was determined by one way ANOVA followed by Tukey's multiple comparison tests using Graph pad prism Version 6.0. Values are represented as Mean ± SEM, Superscript *** denotes p<0.001 vs control, ### denotes p<0.001 respectively, (Aβ: Amyloid beta)

Morphology results

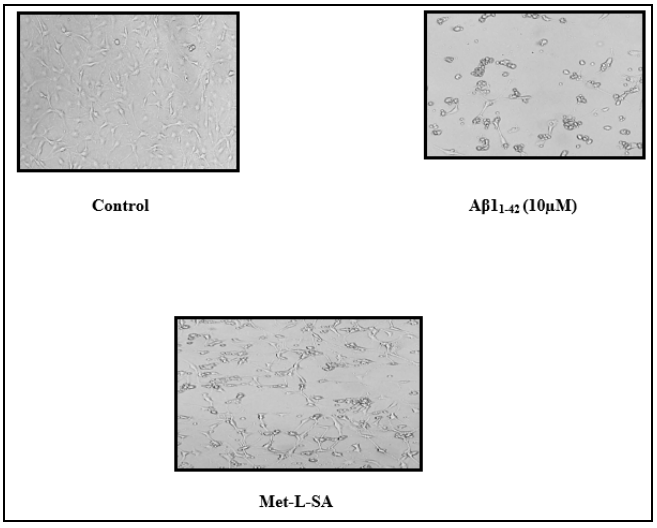

Fig 10

The control SH-SY5Y cells are tiny, highly light retractile, fibroblast-like and good morphological features and growing densely. $A\beta_{1-42}$ (10µM) intoxication caused morphological changes with condensed cell density, swollen, decreased proliferation and differentiation of cells in comparison to the control cells. Post-treatment with met-L-SA extracts have significantly protected the cells from the $A\beta_{1-42}$ toxicity which is evidenced by increased cell density and proliferation. The post-treatment with met-L-SA have shown better morphological restoration.

Discussion

The preliminary phytochemical studies of methanolic extract of leaves of *Senna alata* showed the presence of alkaloids, flavonoids, carbohydrates, protein, terpenoids, tannins, anthraquinone and cardiac glycosides and fatty acids. These phytochemical contstituents identified were further subjected to GC-MS analysis. The GC-MS analysis has shown the presence of 8 compounds such as 4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-, 1-Butanol3-methyl- formate, Methyltetradecanoate, 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, Pentadecanoic acid 14-methyl- methyl ester, 9-Octadecenoic acid, (2-phenyl-1,3-dioxolan-4-yl) methylester, Heptadecanoic acid, 16-methyl-, methyl ester, Heptadecanoic acid, 16-methyl-, methyl ester, Myo-Inositol, 4C-methyl. Among the 8 compounds only some important compounds like Heptadecanoic 16 methyl acid methyl ester, 9-Octadecenoic acid (2-phenyl-1,3-dioxolan-4-yl) methylester, Myo-inositol 4-C methyl were subjected for molecular docking studies. The results have shown that donepezil had the highest binding score -9.2 followed by 9-Octadecenoic acid (2-phenyl-1,3-dioxolan-4-yl) methylester, cis- (-7.7), Heptadecanoic, 16-methyl acid methyl ester (-7.0), Myo-inositol 4-C-methyl (-6.7), Nalpha-(2,4-dinitrophenyl) L-arginine (-6.5). The docked donepezil and the compound molecules were almost found to occupy the same binding site and form similar interactions to those formed by donepezil in the crystal structure, thus confirming the similar activity of the compounds. Inhibition concentration (IC_{50}) of *Senna alata* was found to be 69.77 µg/ml by MTT assay. The percentage of viability of cells was found to be 59.17 in treatment with met-L-SA. *Senna alata* (met-L-SA) on LPO level in Aβ1-42 intoxicated SH-SY5Y cell lines was found to be 62.15, NO level (78.94), GSH level (59.92), SOD (12.87), CAT (0.518), IL- 1β (623.87), TNF-α (675.24). The *in vitro* results showed that the met-L-SA had the potent activity against alzheimer's.

Conclusion

The protein and ligand plays an important role in structural based drug design. In this study phytochemicals obtained from the leaves of *Senna alata* by Gas Chromatography Mass spectrometry (GC-MS) analysis. The presences of different bioactive compounds provide effective use of plant parts for various ailments by traditional specialists. In this work AChE docked against the phytochemical constituents of *Senna alata* leaves and 9-Octadecenoic acid (2-phenyl-1, 3-dioxolan-4-yl) methylester, cis- (-7.7), Heptadecanoic, 16-methyl acid methyl ester (-7.0), Myo-inositol 4-C-Methyl (-6.7) were found to be promising lead targets against alzheimer's based on molecular docking analysis. So, *in vivo* approaches are therefore recommended to elucidate the molecular mechanism of these compounds to act as potent drugs against alzheimer's.

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