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Molecular docking based screening of GABA (A) receptor inhibitors from plant derivatives

Mohammed Marunnan Sahila[1, 2], Pallikkara Pulikkal Babitha[3], Srinivas Bandaru[4], Anuraj Nayarisseri[4] & Victor Arokia Doss[5]*

[1]Department of Bioinformatics, School of Life Sciences, Karpagam University, Coimbatore 641021, India; [2]Department of Bioinformatics, SIAS-Centre for Scientific, Research, Safi Institute of Advanced Study(SIAS) , Rasiya Nagar, Vazhayoor East, Malappuram-673633, Kerala, India; [3]Research and Development centre, Bharathiyar University,Coimbatore.641046,Tamilnadu; [4]Bioinformatics Research Laboratory, Eminent Biosciences, Vijaynagar, Indore - 452010, India; [5]Department of Biochemistry, PSG College of Arts and Science, Coimbatore - 641 014, India; Victor Arokia Doss – Email: victordoss64@hotmail.com; *Corresponding author

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Abstract:
The present antipsychotic drugs have known to show serious concerns like extra pyramidal side effects therefore, pursuit for novel antipsychotic GABAnergic drugs has lately focused on the folkloric medicine from plant derivatives as better treatment option of schizophrenia. The present study centers to identify potential inhibitors of plant origin for GABA receptor through in silico approaches. Three compound datasets were undertaken in the study. The first set consisted of seven compounds which included Magnolol, Honokiol and other plant derivatives. The second set consisted of 16 derivatives of N-diarylalkenyl-piperidinecarboxylic acid synthesized by Zheng *et al.,* 2006. The third dataset had thirty two compounds which were Magnolol and Honokiol analogues synthesized by Fuchs *et al.,* 2014. All the compounds were docked at the allosteric site of the GABA (A) receptor. The compounds were further tested for ADMET and biological activity. We observed Honokiol and its derivatives demonstrated superior druglike properties than any compound undertaken in the study. Further, compound 61 [2-(4-methoxyphenyl)-4-propylphenol] of dataset three - a synthetic derivative of honokiol had better profile than its parent compound. In a possible attempt to identify compound with even better efficacious compound than 61, virtual screening was performed, 135 compounds akin to compound 61 were retrieved. Interestingly none of the 135 compounds showed better druggable properties than compound 61. Our in silico pharmacological profiling of compounds is in coherence and is complemented by the findings of Fuchs *et al*, which also revealed compound 61 to be the good potentiator of GABA receptor.

Keywords: Schizophrenia, Plant derivatives, GABA inhibitors, *in silico* Pharmacological profiling

Abbreviations: GABA (A) R: Gamma Amino Butyric Acid Receptor, subtype A; GPCR: G Protein Coupled Receptor; OPLS: Optimized Potentials for Liquid Simulations; PDB: Protein Data Bank; PLP: Piece wise Linear Potential; T.E.S.T: Toxicity Estimation Software Tool; TCM: Traditional Chinese Medicine

Background:
Schizophrenia is a heterogenous neurodevelopmental disorder characterized by hallucinations; psychotic thought patterns of neural communication, which contribute to behavioral changes **[1, 2]** and impaired sensory processing **[3-6].** GABAnergic system is principally involved in the balance of excitation and inhibition in the brain. Involvement of GABAnergic system in pathogenesis of schizophrenia comes from the compelling evidence wherein prenatal exposure to infection significantly increases immune reactivity of α2 subunit of GABAA receptor in rat cortico-limbic structures resulting in elevating the incidence of schizophrenia **[7].** Apparently, binding studies have shown increased binding of high affinity [3H]GABA to the total population of GABAA receptors in post-mortem

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schizophrenic brains compared with controls **[8-14].** Ubiquitous presence of GABA receptors makes almost all the neurons to release GABA [15] and for this reason it is expected that most brain functions involve GABAnergic transmission **[15]** therefore forms an important drug target in neurological disorders.

In spite of tremendous progress made in confronting the disease, the present pharmacological properties that confer the therapeutic effects on GABAnergic system have remained elusive and certain side effects still impacts patient health and quality of life. In certain cases the present medication often produces psychotomimetic responses in humans and has lead to hypersensitivity in patients **[16-17].** For example conventional antipsychotics like as haloperidol, has been associated with higher rate of extra pyramidal side effects. Considering the serious side effects of conventional antipsychotics a new antipsychotics like Olanzapine, Amisulpride, Clozapine and Risperidone were launched which presumed to been highly effective. In spite of being efficacious and providing better treatment schizophrenic symptomatology, modern antipsychotics still suffer side effects **[18]**. For example, Clozapine is an effective treatment for those who respond poorly to other drugs, **[19]** but it has potentially serious side effect of agranulocytosis (lowered white blood cell count) in less than 4% of people **[20].** People on typical antipsychotics tend to have a higher rate of extra pyramidal side effects while some atypicals are associated with considerable weight gain, diabetes and risk of metabolic syndrome; this is most pronounced with Olanzapine, while Risperidone has a similar rate of extrapyramidal symptoms to conventional drug - haloperidol **[19].** It remains unclear whether the newer antipsychotics reduce the chances of developing neuroleptic malignant syndrome or tardive dyskinesia, but however poses a threat in clinical management of schizophrenia **[21].** Deemed to such serious side effects, the American Psychiatric Association suggests considering stopping antipsychotics in some people if there are no symptoms for more than a year **[22].** Owing to serious concerns that present medication offers and efficacy being limited, research is being majorly focused to design novel drugs bestowed to overcome the side effects that current anti psychotics suffer.

The pursuit for novel antipsychotic GABAnergic drugs has lately focused on the plant derivatives bestowed with potential to treat psychotic disorder especially medicinal plants used in folkloric or traditional medicine like Traditional Chinese Medicine (TCM). Throughout the long Chinese history, there has been an accumulation of experience using medicinal plants to treat a variety of psychotic diseases. For example Honokiol and Magnolol obtained from Magnolia officinalis is well known antidepressant and shows anxiolytic effects. In addition many flavonoids, such as apigenin, chrysin and amentoflavone, have been purified from plants and shown to treat disorders of central nervous system in vitro **[23].**

In the given view, the present study centers to identify plant derivative as a potential inhibitor for GABAA receptor bestowed with least toxicity, high affinity and appreciable pharmacological properties for the clinical treatment of schizophrenia.

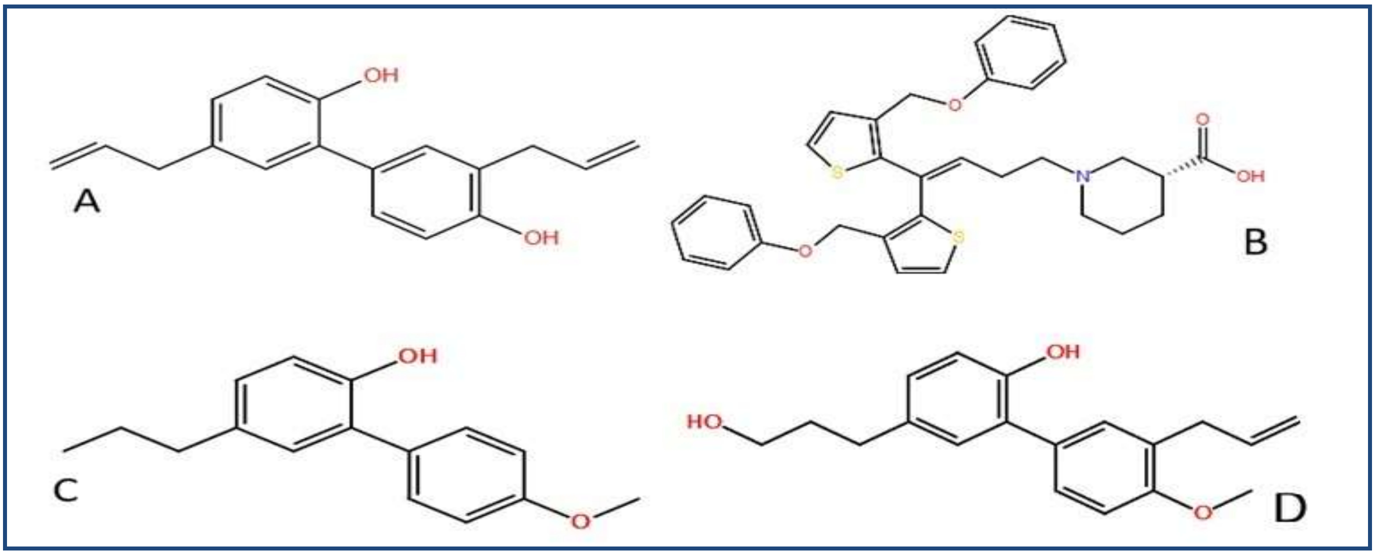

Figure 1: Structure of best docked compound from each dataset **(A)** Honokiol (dataset -1) **(B)** 4e [(3R)-1-{4,4-bis[3-(phenoxymethyl)thiophen-2-yl]piperidine-3-carboxylic acid] (Dataset 2) **(C)** 61 [2-(4-methoxyphenyl)-4-propylphenol](Dataset 3) **(D)** AGN-PC-0DAHLN- molecule similar to compound 61 of dataset 3

Methodology:

Dataset selection

Three sets of compounds were evaluated for their pharmacological profile in the study. Set 1 **Table 1 (see supplementary material)** consisted of established potent GABAA receptor inhibitors of plant origin like Acacetin, Saikosaponin A, Rutaecarpine, Flunitrazepam, Honokiol, Magnolol, 6-methylflavone. Set 2 **Table 2 (see supplementary material)** consisted of sixteen compounds belonging to N-diarylalkenyl-piperidinecarboxylic acid derivatives designed by Zheng *et al.*, 2006 **[24]** and finally set 3 **Table 3 (see supplementary material)** consisted of thirty two plant compound analogues of Magnolol and Honokiol proposed by Fuchs *et al.*, 2014 **[25].**

Preparation of protein and compounds

The crystal structure of GABA (A) receptor was retrieved from Protein Data Bank (PDB) with PDB ID: 4COF **[26].** The X-Ray

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diffraction structure of GABA (A) receptor had a resolution of 2.97 Å, R value of 0.206 and R free value of 0.226. Unit cell parameters were as Length [Å] a = 174.10, b = 108.90, c = 207.44, Angles [°] α = 90.00, β = 107.43, γ = 90.00. The structure was downloaded in .pdb format and was further prepared for docking process. The protein was prepared using the PrepWiz module of Schrodinger suite **[27].** In the preparation procedure, the protein was first preprocessed by assigning the bond orders and hydrogen, creating zero order bonds to metals and adding disulphide bonds. The missing side chains and loops were filled using Prime Module of Schrodinger. Further all the water molecules were deleted beyond 5 Å from hetero groups. Once the protein structure was preprocessed, H bonds were assigned which was followed by energy minimization by OPLS 2005 force field. The final structure obtained was saved in.pdb format for further studies. All the ligands were optimized through OPLS 2005 force field algorithm **[28]** embedded in the LigPrep module of Schrödinger suite, 2013 (Schrodinger. LLC, New York, NY). The ionizations of the ligand were retained at the original state and were further desalted. The structures thus optimized were saved in .sdf format for docking procedures **[29].**

Structure Similarity search
The compound with superior pharmacological profile amongst all the datasets was further used as query molecule in pursuit to identify still better druglike compound than any molecules mentioned in the dataset. Similarity search was supervised by Binary Finger Print Based Tanimoto similarity equation to retrieve compounds with similarity threshold of 95 % against NCBI's Pubchem compound database.

Molecular docking of compounds
Molecular docking program- Molegro Virtual Docker (MVD) which incorporates highly efficient PLP (Piece wise Linear potential) and MolDock scoring function provided a flexible docking platform **[30].** All the ligands were docked at the allosteric site of the GABAA receptor with reference to co-crystallized ligand- benzamidine, present in the protein structure (Coordinates: x= -20.558, y= -19.574 and z= 127.994). Docking parameters were set to 0.20Å as grid resolution, maximum iteration of 1500 and maximum population size of 50. Energy minimization and hydrogen bonds were optimized after the docking. Simplex evolution was set at maximum steps of 300 with neighborhood distance factor of 1. Binding affinity and interactions of ligands with protein were evaluated on the basis of the internal ES (Internal electrostatic Interaction), internal hydrogen bond interactions and sp2-sp2 torsions. Post dock energy of the ligand-receptor complex was minimized using Nelder Mead Simplex Minimization (using non-grid force field and H bond directionality) **[31].** On the basis of rerank score best interacting compound was selected from each dataset.

Bioactivity and ADMET profiling of compounds
All the compounds were screened for its drug ability by lipinksi filters. Biological activity of the ligands was predicted using Molinspiration webserver (© Molinspiration Cheminformatics 2014). LC 50 was predicted using T.E.S.T. Version 4.1 (2012, U.S. Environmental Protection Agency) software. The complete ADMET properties was calculated using admetSAR **[32].**

Pharmacophoric Mapping
Pharmacophoric mapping which involves ligand interaction patterns, hydrogen bond interaction, hydrophobic interactions was evaluated using Accelrys Discovery Studio 3.5 DS Visualizer **[33, 34].**

Softwares, Suites and Webservers used
All the chemical structures were drawn in MarvinSketch 5.6.0.2, (1998-2011, Copyright © ChemAxon Ltd). Ligands were optimized with LigPrep module of Schrodinger suite 2013. Protein was processed and refined with protein preparation wizard of Schrodinger suite 2013 (Schrodinger. LLC, 2009, New York, NY). Flexible molecular docking of the compounds with target was completed using Molegro Virtual Docker 2010.4.0.0. Accelrys Discovery Studio® Visualizer 3.5.0.12158 (Copyright© 2005-12, Accelrys Software Inc.) was used for molecular visualizations. T.E.S.T software (2012, U.S. Environmental Protection Agency) and Molinspiration web server (© Molinspiration Cheminformatics 2014) were respectively used for predicting LC50 and bioactivity of the compound. ADMET profiles were calculated using admetSAR (Laboratory of Molecular Modeling and Design. Copyright @ 2012, East China University of Science and Technology, Shanghai Key Laboratory for New Drug Design,).

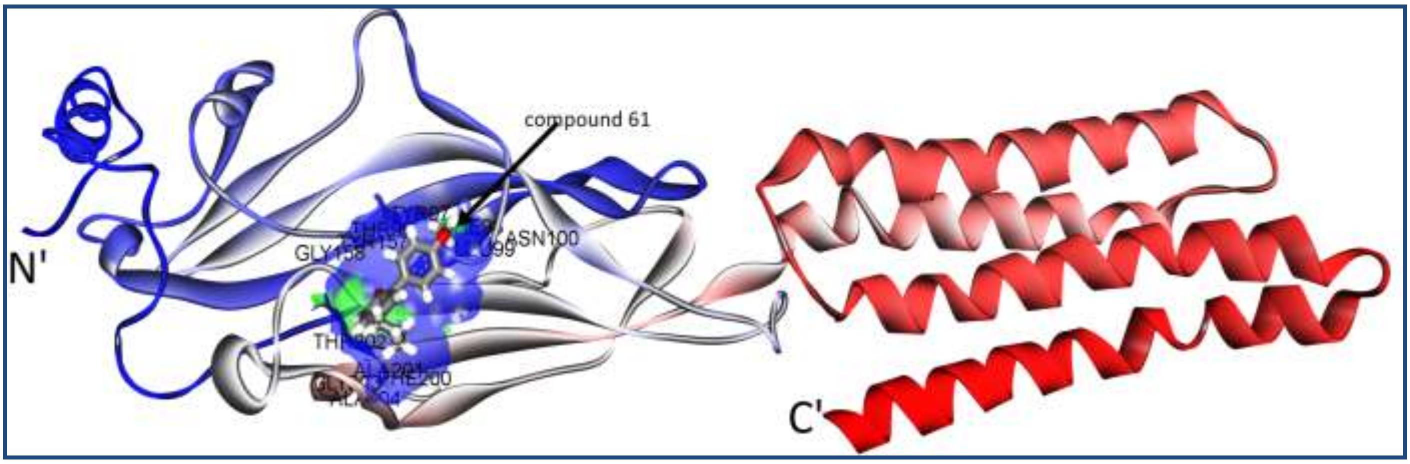

Figure 2: Compound 61 of dataset 3 bound at the active site. (Active site represent as solvent accessible surface area. Blue shade represents high solvent accessible surface area, green shade is vice- versa).

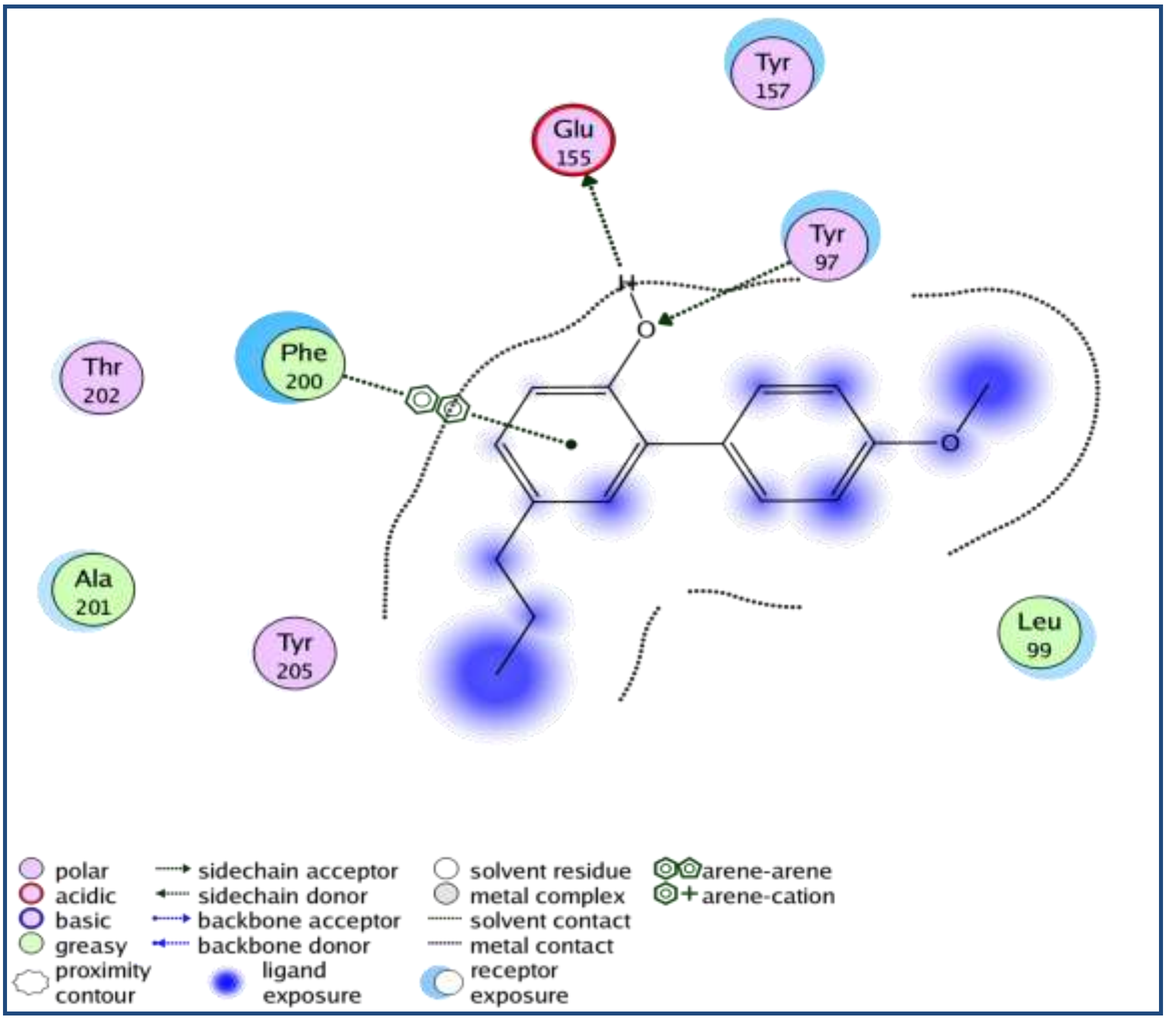

Figure 3: Interactions of compound 61 in the allosteric site of the GABAA receptor. Residues circled in green participate in van der Waals interaction (labeled as greasy) with the ligand while residues in pink forms electrostatic interactions (labeled as polar residues). The dotted line around the ligand represents periphery of the active site. Hydrogen bonds formed by compound 61 with residues Glu 155 and Tyr 97. The arene-arene (п- п) interactions are established between compound 61 and Phe 200.

Results & Discussion:

Table 4 shows the best docked compound from each dataset. Evident from the docking (rerank) scores Honokiol **(Figure 1a)** from dataset 1, compound 4e **(Figure 1b)** from dataset 2 and compound 61 **(Figure 1c)** belonging dataset 3 showed highest affinity. Compound 61 derivative of Honokiol demonstrated highest binding affinity against GABAA receptor than any compound in the either sets. In addition, Compound 61 from dataset 3 shows 1.21 folds increased affinity than its parent compound Honokiol. The superior affinity of compound 61 can be attributed to its excellent interaction profile especially in terms of electrostatic and H-bonding interactions. Apparent from the docking profile of compound 61 energy values of descriptors of external ligand interactions contributes 7.32 folds higher stability than internal ligand interactions. Further external ligand interactions were stabilized mostly by steric energy guided by Piece wise linear potentials. While in internal ligand interactions, the torsional strain contributes for the stability of the ligand receptor interactions.

In further approach, in pursuit to identify even better molecule endowed with superior pharmacological profile than compound 61, virtual screening was performed against Pubchem database (taking compound 61 as query). A total of 135 compounds structurally similar to compound 61 were retrieved. All the 135 compound retrieved hitherto was docked against GABA receptor. Compound AGN-PC-0DAHLN (CID: 60152869) **(Figure 1d)** showed superior binding affinity out of all the 135 compounds **Table 4 (see supplementary material)**, further also showed appreciable pharmacological profile.

It is interesting to note that, none of the 135 virtually screened compounds showed better binding affinity or pharmacological profile than its parent compound 61. Compound 61 demonstrated 1.30 folds better affinity than its best docked similar compound AGN-PC-0DAHLN (CID: 60152869). In addition compound 61 had better pharmacological profile than its similar AGN-PC-0DAHLN (CID: 60152869). Compound 61 in the active site is shown in **Figure 2.**

The ADMET profiles **Table 5 (see supplementary material)** of the best docked compound belonging to each of the three datasets and compound 61 akin AGN-PC-0DAHLN revealed that compound 61 was better compound and most likely druglike compared to its parent compound honokiol and to its similar AGN-PC-0DAHLN. The predicted bioactivity **Table 6 (see supplementary material)** as well as the LC 50 values of compound 61 was quite appreciable. The LC 50 value at 96 hour interval was predicted to be 4.6 folds superior for compound 61 than its parent compound honokiol and 1.6 folds better than its similar AGN-PC-0DAHLN. Compound 4e from dataset 2 also showed good binding profiles and ADMET properties but was somewhere intermediate between honokiol and its analogue compound 61. In addition all the compounds identified showed enhanced bioactivity providing a clue for target specificity. The pharmacological profiles of the entire three best docked compounds and compound 61 similar AGN-PC-0DAHLN were although appreciable, but it was compound 61 which showed best amongst all the compounds studied in different datasets and therefore it was further analyzed for pharmacophoric mappings.

Comprehensively shown in **Figure 3**, the compound 61 demonstrates van der Waals interactions with Ala 201, Phe 200, Leu 99, and electrostatic interactions with Tyr 157 & 97, 205 and Thr 202. Compound 61 is a hydrogen bond donor from electrostatic residues Tyr 97 and donor to Glu 155. Electrostatic and hydrophobic interactions of compound 61 in the site is shown in **Figure 4a** and **Figure 4b** respectively.

It is interesting to note that, findings by Fuchs *et al*., 2014 also showed that compound 61 was the best potentiator of GABA (A) receptor in *Xenopus laevis* defolliculated oocytes. Compound 61, increased the GABA-induced current by 5000 % at 10 µM concentration making it the best allosteric potentiator **[20]**. Owing to the coherence of our Insilco pharmacological profiling to bioactivity profiling by Fuchs *et al.,* it can be anticipated that compound 61 may form potential allosteric GABA receptor inhibitor in the clinical treatment of schizophrenia. In addition, in a possible attempt to identify better compound than 61, we performed virtual screening process and ended up by retrieving 135 compounds. Contrary to our expectation, none of the 135 similar compounds retrieved showed appreciable pharmacological profile than its parent compound 61, testifying compound 61 to be best allosteric modulator of GABA receptor hitherto discovered.

Two thirds of previous studies reported positive results using GABA inhibitors, while, one third reported either no difference or a negative response. The negative results involved Excessive sedation, Cognitive impairment, Ataxia, Dysarthria, Postural hypertension, Worsening of psychosis, Hyperarousal, "Paradoxical" agitation and Respiratory depression, in addition, the regular use of the GABA inhibitors in some patients lead to cumulative toxicity **[35].**

From our study we anticipate compound 61 can be an ideal inhibitor against GABA which can be put forth for pharmacodynamic and pharmacokinetic experiments and potentially overcome narrow therapeutic window of currently available GABA inhibitors in the successful treatment of schizophrenia.

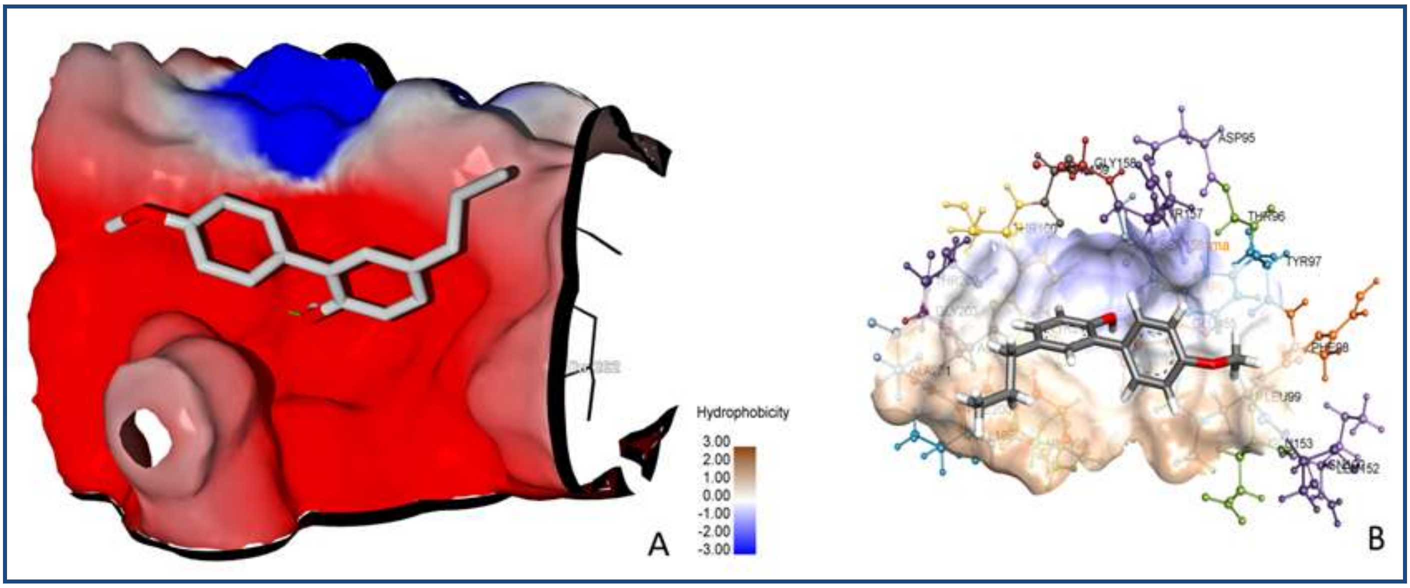

Figure 4: (A) Compound 61 deeply embedded in the allosteric site surrounded by highly electronegative residues. **(B)** The site harboring compound 61 is shown with hydrophobic intensities. The hydrophobic intensities of the binding site ranges from -3.00 (least hydrophobic area - blue shade) to 3.00 (highly hydrophobic area –brown shade).

Conclusion:

Narrow therapeutic window of available GABA inhibitors necessitates an urgent need to develop new drugs treatment of schizophrenia. Therefore in the given view we identified compounds derived from plant source with optimal pharmacological profile. In the study, Honokiol and its analogue compound 61 synthesized by Fuchs *et al.,* 2014 demonstrated drug like properties endowed with higher binding affinity, least toxicity and optimal bioactivity. The optimal binding affinity of compound 61 unlike other compounds undertaken in the study can be attributed for its optimal electrostatic interactions in the active site of GABA (A) receptor. In addition, compound 61 also showed better bio-availability, target specificity and least LC50 values testifying it to be better compound than rest of the compounds analyzed in the study. Our study demonstrating optimal pharmacological profile of compound 61 is complimented by findings by Fuchs et al. 2014 which also showed compound 61 to be a superior potentiator of GABA receptor.

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Supplementary material:

Table 1: Compounds of set 1. GABA (A) receptor inhibitors of plant origin

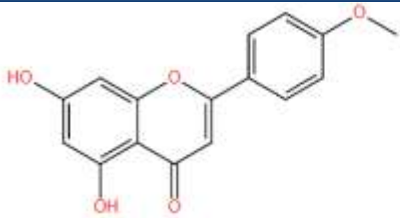
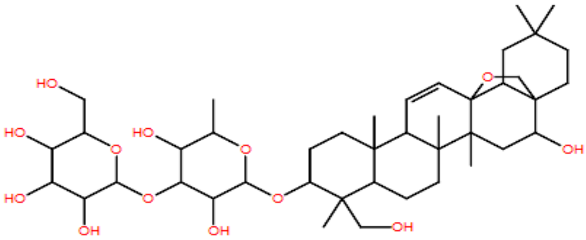
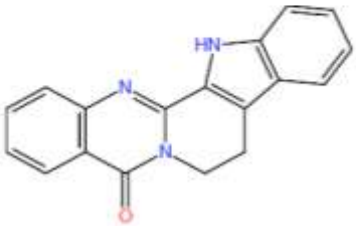
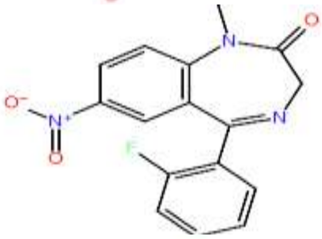
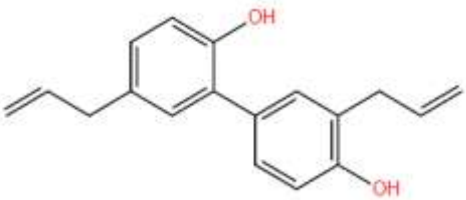
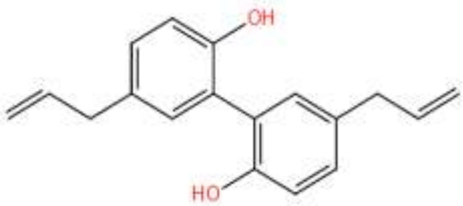
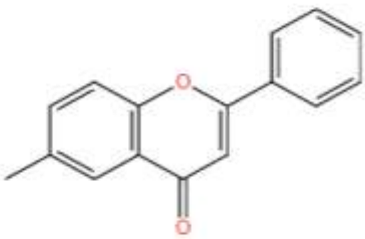
Compound	Structure	PubChem ID
Acacetin ($C_{16}H_{12}O_5$)		5280442
Saikosaponin A ($C_{42}H_{68}O_{13}$)		107793
Rutaecarpine ($C_{18}H_{13}N_3O$)		65752
Flunitrazepam ($C_{16}H_{12}FN_3O_3$)		3380
Honokiol ($C_{18}H_{18}O_2$)		72303
Magnolol ($C_{18}H_{18}O_2$)		72300
6-methylflavone ($C_6H_{12}O_2$)		689013

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Table 2: Compounds of dataset 2 - N-diarylalkenyl-piperidinecarboxylic acid derivatives designed by Zheng *et al*., 2006

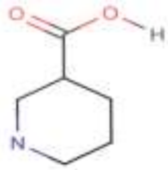
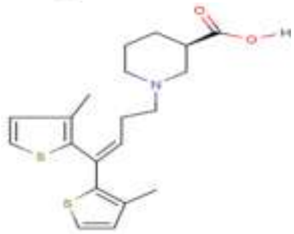
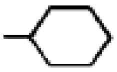
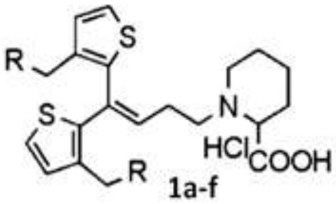
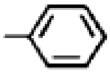
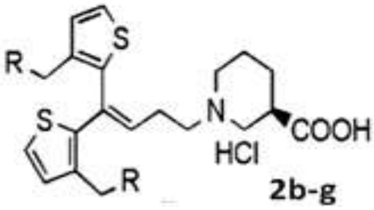
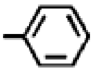
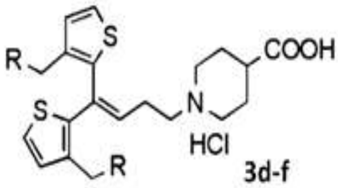
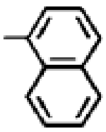
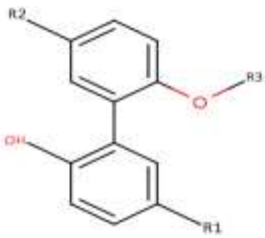
Compound	Core structure	Substituent
1_NIPECOTIC ACID		R: a =H, b =-OCH_3,
2_TIAGABINE		c =-$OCH(CH_3)_2$, d =-O 
1a **1b** **1d** **1e** **1f**		e =-O 
2b **2c** **2d** **2e** **2f** **2g**		f =-OCH_2 
3d **3e** **3f**		g =-O 

Table 3: Compounds of dataset 3 analogues of Magnolol and Honokiol designed by Fuchs et al., 2014

Series I. Magnolol Analogues (37-58)



Compound Number	R¹	R²	R³
37	H	pentyl	H
38	H	hexyl	H
39	methyl	butyl	H
40	methyl	pentyl	H
41	methyl	hexyl	H
42	ethyl	propyl	H
43	ethyl	butyl	H
44	ethyl	pentyl	H

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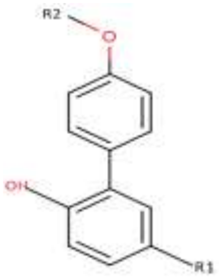
45	ethyl	hexyl	H
46	propyl	pentyl	H
47	propyl	hexyl	H
48	propyl	heptyl	H
49	propyl	octyl	H
50	butyl	pentyl	H
51	butyl	hexyl	H
52	ethyl	pentyl	CH_3
53	ethyl	hexyl	CH_3
54	propyl	pentyl	CH_3
55	propyl	hexyl	CH_3
56	pentyl	ethyl	CH_3
57	pentyl	propyl	CH_3
58	hexyl	propyl	CH_3

Series II. 4′-O-methyl Honokiol Analogues (59-69)



59	methyl	methyl	-
60	ethyl	methyl	-
61	propyl	methyl	-
62	butyl	methyl	-
63	pentyl	methyl	-
64	hexyl	methyl	-
65	heptyl	methyl	-
66	octyl	methyl	-
67	hexyl	ethyl	-
68	hexyl	propyl	-
69	hexyl	isopropyl	-

Table 4: Affinity (Rerank) scores of the best docked compound from each set. Compound 61 a derivative of Honokiol of set 3 demonstrates highest affinity relative to all the compounds in included in three datasets.

Best docked compound in the dataset	**Honokiol Dataset 1**	**4e Dataset 2**	**61 Dataset 3**	**AGN-PC-0DAHLN (CID: 60152869 Virtual screened compound (query compound 61)**
Energy overview: Descriptors	**Rerank Score**	**Rerank Score**	**Rerank Score**	**Rerank Score**
Total Energy	-68.625	-77.043	-85.856	-66.023
External Ligand interactions	-76.07	-85.708	-99.421	-80.025
Protein - Ligand interactions	-76.07	-85.708	-99.421	-80.025
Steric (by PLP)	-60.728	-66.421	-73.789	-57.674
Steric (by LJ12-6)	-12.754	-15.391	-19.214	-14.43
Hydrogen bonds	-2.588	-3.896	-6.418	-7.92
Internal Ligand interactions	7.445	8.665	13.564	14.001
Torsional strain	0.226	1.366	11.444	3.167
Steric (by PLP)	0.692	0.347	-6.3	2.094

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Table 5: ADMET profile calculated for best docked compound from each dataset by admetSAR

	Honokiol (dataset1)		4e (dataset 2)		61 (dataset 3)		AGN-PC-0DAHLN	
	Result	**probability**	**Result**	**probability**	**Result**	**probability**	**Result**	**probability**
Absorption								
Blood-Brain Barrier	BBB+	0.8252	BBB+	0.8813	BBB+	0.9099	BBB+	0.5259
Human Intestinal Absorption	HIA+	1	HIA+	0.8396	HIA+	1	HIA+	0.9959
Caco-2 Permeability	Caco2+	0.8273	Caco2-	0.6107	Caco2+	0.8947	Caco2+	0.7514
P-glycoprotein Substrate	Non-substrate	0.6836	Substrate	0.7351	Non-substrate	0.6096	Substrate	0.5373
Renal Organic Cation Transporter	Non-inhibitor	0.8431	Inhibitor	0.7258	Inhibitor	0.8012	Non-inhibitor	0.764
Distribution & Metabolism								
CYP450 2C9 Substrate	Non-substrate	0.7833	Non-substrate	0.7795	Non-substrate	0.7439	Non-substrate	0.7551
CYP450 2D6 Substrate	Non-substrate	0.8724	Non-substrate	0.6487	Non-substrate	0.733	Non-substrate	0.7955
CYP450 3A4 Substrate	Non-substrate	0.6852	Non-substrate	0.5	Non-substrate	0.5	Substrate	0.5057
CYP450 1A2 Inhibitor	Inhibitor	0.7059	Inhibitor	0.5413	Inhibitor	0.8583	Inhibitor	0.6581
CYP450 2C9 Inhibitor	Inhibitor	0.7918	Non-inhibitor	0.6553	Non-inhibitor	0.5298	Non-inhibitor	0.7653
CYP450 2D6 Inhibitor	Non-inhibitor	0.9043	Non-inhibitor	0.5946	Non-inhibitor	0.7733	Non-inhibitor	0.8931
CYP Inhibitory Promiscuity	High CYP Inhibitory Promiscuity	0.8978	High CYP Inhibitory Promiscuity	0.7136	High CYP Inhibitory Promiscuity	0.7423	High CYP Inhibitory Promiscuity	0.6216
Excretion & Toxicity								
Human Ether-a-go-go-Related Gene Inhibition	Weak inhibitor	0.8689	Strong inhibitor	0.5379	Weak inhibitor	0.8224	Weak inhibitor	0.8318
AMES Toxicity	Non AMES toxic	0.8786	Non AMES toxic	0.7975	Non AMES toxic	0.9438	Non AMES toxic	0.8479
Carcinogens	Non-carcinogens	0.806	Non-carcinogens	0.9648	Non-carcinogens	0.7676	Non-carcinogens	0.8934
Acute Oral Toxicity	III	0.5821	III	0.5416	III	0.7779	III	0.7502

Table 6: Predicted LC 50 and bioactivity of compounds

		Lethal Dose Concentration	Bioactivity					
Compound dataset	**compound with best docking profile in dataset**	**LC50 (96 hr) mg/L**	**GPCR ligand**	**Ion channel modulator**	**Kinase inhibitor**	**Nuclear receptor ligand**	**Protease inhibitor**	**Enzyme inhibitor**
Set 1	Honokiol	0.12	0.03	0.06	-0.08	0.32	-0.2	0.13
Set 2	4e	0.17	0.25	-0.11	-0.15	0.12	0.14	0.15
Set 3	61	0.56	-0.01	0.04	-0.14	0.23	-0.21	0.06
Virtually screened compound	AGN-PC-0DAHLN	0.35	-0.15	0.05	-0.01	0.43	-0.08	0.16

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