ISSN: 2322 - 0902 (P)
ISSN: 2322 - 0910 (O)

International Journal of Ayurveda and Pharma Research

Research Letter

IN SILICO TARGET IDENTIFICATION OF NOOTROPIC BIOACTIVE COMPOUNDS FROM AYURVEDIC HERBS

Suresh A. Poovathinal[1], Ayyappan Anitha[2]*, Premjith Puliyappatta[3], Vijitha Viswambharan[2], Ismail Thanseem[2]

[1]Dept. of Neurology, *[2]Dept. of Neurogenetics, [3]Integrated Medical Research, Institute for Communicative and Cognitive Neurosciences (ICCONS), Shoranur, Palakkad, Kerala, India.

ABSTRACT

Numerous plants are listed in the Ayurvedic pharmacopoeia, and several different plant parts are being used in Ayurvedic formulations. The bioactive ingredients of many of these medicinal have been identified. A key step in Ayurvedic drug development is the identification and validation of biological targets of these bioactive ingredients. Most of the experimental techniques involving genomic, proteomic and metabolomic approaches for target identification are laborious and expensive. Computational approaches allow an efficient alternative approach for *in silico* target prediction of bioactive compounds. Here, we have used computational methods to predict the target proteins of major bioactive compounds present in seven medicinal plants (*Bacopa monnieri, Centella asiatica, Clitoria ternatea, Acorus calamus, Glycyrrhiza glabra, Celastrus paniculatus, Nardostachys jatamansi)* known for their nootropic properties. These plants/plant parts are being used in various traditional Ayurveda formulations intended for cognitive enhancement and memory boosting. Even though these plants are widely used in the treatment of cognitive deficits, their scientific evaluation is lacking. Till date, very few studies have attempted to elucidate the targets or to explain the mode of action of bioactive ingredients in nootropic medicinal plants. We have chosen three databases for target prediction- ChEMBL, Swiss Target Prediction, and Binding DB. Based on available literature, we also examined if any of the predicted target proteins have brain-related functions. Pertinent *to* the nootropic properties of the medicinal plants, our study revealed several potential target proteins such as *CYP19A1*, MAPT, PTGS1, ACHE, *SLC6A2*, SLC6A3, MAOA and MAOB implicated in neurodevelopment, neuroprotection, learning and memory.

KEYWORDS: Ayurveda, Cognition, Nootropic, Target prediction.

INTRODUCTION

Ayurveda, which means "science/knowledge of life", is a traditional system of alternative medicine in India making use of medicinal plants. Ayurveda is well renowned for its efficacy in the treatment of a variety of diseases and conditions including asthma, arthritis, rheumatism, skin diseases, spondylosis, gastric problems, neurological disorders and paralysis.

Numerous species of plants are listed in the Ayurvedic pharmacopoeia, and different types of plant parts are used in Ayurvedic formulations. The pharmacologically active (bioactive) ingredients of many medicinal plants used in Ayurveda have been identified. A key step in this process is target identification and validation. [1] There is a range of genomic, proteomic and metabolomic techniques that predicts or explains the mode of action of bioactive compounds. [2,3] However, such experimental techniques have been laborious and expensive. Novel computational approaches such as *in silico* target prediction is a well-established alternative approach for predicting the targets of bioactive compounds. [4-6]

Here, we have used computational methods to predict the target proteins of major bioactive compounds present in 7 medicinal plants that are known for their nootropic properties. These plants/plant parts are being used in various traditional Ayurveda formulations such as *Saraswatharishta, Brahma rasayana, Brahmi ghrita and Manasamitra vadakam*, intended for cognitive enhancement and memory boosting. Cognitive deficits in neurodevelopmental and neurodegenerative disorders demand the use of nootropics to boost cognitive abilities. Ayurvedic drugs prepared from these plants have been found to possess anti-inflammatory properties, have a calming effect on the central nervous system, and act as nootropics enhancing memory, learning and other cognitive functions. [7] Even though these plants and their formulations are widely used in the treatment of cognitive deficits, their scientific evaluation is lacking. Till date, very few studies have attempted to elucidate the targets or to explain the mode of action of bioactive ingredients in nootropic medicinal plants.

Materials and Methods

A list of medicinal plants selected for this study is given in Table 1.

Table 1: Medicinal plants with nootropic activity

Botanical name	Local name	Useful part	Pharmacological activity	References
Bacopa monnieri	*Brahmi*	Whole plant	Cognitive enhancement	[39]
Centella asiatica	*Kudangal*	Whole plant	Memory enhancement	[40]
Clitoria ternatea	*Sankupushpam*	Root	Brain tonic; enhancement of memory and intelligence	[41]
Acorus calamus	*Vayambu*	Root	Memory enhancement	[42]
Glycyrrhiza glabra	*Earattimaduram*	Root	Memory improvement	[43]
Celastrus paniculatus	*Jyothishmathi*	Seed	Cognitive enhancement; memory improvement	[44]
Nardostachys jatamansi	*Jatamanchi*	Rhizome	Improvement of memory and learning; neuroprotective	[45,46]

Three databases were chosen for target prediction, viz. ChEMBL (https://www.ebi.ac.uk/chembl/), Swiss Target Prediction (http://www.swisstargetprediction.ch/) and Binding DB (https://www.bindingdb.org/bind/index.jsp). Target prediction in these databases is based on the chemical structure of the bioactive ingredient which was provided as simplified molecular-input line-entry system (SMILES), a line notation representing molecules. Based on available literature, we also examined if any of the predicted target proteins have brain-related functions or has been implicated in neurological disorders.

Results and Discussion

The predicted target proteins of various bioactive ingredients of the 7 medicinal plants are listed in Table 2.

Table 2. Bioactive ingredients of medicinal plants and their predicted target proteins

Botanical name	Bioactive compound	Chemical nature	Molecular formula	Target prediction		
				ChEMBL	Swiss Target	BindingDB
Bacopa monnieri	Bacoside A,B	Triterpenoid Saponin	$C_{41}H_{68}O_{13}$		FLT1 FLT4 KDR	ATP1A1 HSD11B1 HSD11B2 KLF5 LYST NR3C1
Centella asiatica	Asiaticoside	Triterpene glycoside	$C_{48}H_{78}O_{19}$	PYGM		F2 STAT1 STAT2 STAT3 STAT4
Clitoria ternatea	Taraxerol	Triterpenoid	$C_{30}H_{50}O$	NOS2	ACHE **AR** BCHE **CYP19A1** **CYP51A1** **HMGCR** LDLR LRP8 **PTPN1** PTPN2 SLC6A2 SLC6A3 SLC6A4 TDP1 VLDLR	**AR** **CYP19A1** **CYP51A1** **HMGCR** **PTPN1**
	Taraxerone	Triterpenoid	$C_{30}H_{48}O$	NOS2	CYP17A1 **CYP19A1** **ESR1** ESR2 FAAH **MAPT** MBNL1 MBNL2 MBNL3	**CYP19A1** **ESR1** **MAPT** **PTGS1** **PTGS2**

					NR3C1 NR3C2 **PTGS1** **PTGS2** SRD5A1 SRD5A2	
Acorus calamus	α-asarone β-asarone	Ether	$C_{12}H_{16}O_3$	CYP3A4 CYP2D6 HMGCR	**CYP19A1** **ESR1** ESR2 GFER **MAPT** NQO1 **NQO2** MAOA MAOB MC1R **PTGS1** **PTGS2** **TUBB1** TUBB8	ABCB1 ABCG2 AHR ALOX5AP APP CYP1A1 CYP1A2 **CYP19A1** CYP1B1 **ESR1** **MAPT** **NQO2** **PTGS1** **PTGS2** TUBB **TUBB1** XIAP
Glycyrrhiza glabra	Glycyrrhetic acid	Triterpenoid	$C_{30}H_{46}O_4$	**AKR1B1** **AKR1B10** **CYP1A2** CYP2D6 CYP2C9 CYP2C19 CYP3A4 GMNN **HSD11B1** **HSD11B2** HSD17B1 HSD17B2 LMNA MAPT POLK PPARG PRKCD **PRKCH** **PTPN1** **PTPN2** **PTPN6** PTPN7 **PTPN11** RHO **SLCO1B1** **SLCO1B3**	AKR1A1 **AKR1B1** **AKR1B10** AKR1B15 AKR1E2 **AR** **HSD11B1** HSD11B1L **HSD11B2** PRKCE **PRKCH** **PTPN6** **PTPN11**	**AKR1B10** **AR** **CYP1A2** **HSD11B1** **HSD11B2** **PRKCH** **PTPN1** **PTPN2** **PTPN11** **SLCO1B1** **SLCO1B3**
	Glycyrrhizin	Saponin glycoside	$C_{42}H_{62}O_{16}$	**HSD11B1** **HSD11B2** **NR3C1** **PTPN1**	**HSD11B1** HSD11B1L **HSD11B2**	**HSD11B1** **HSD11B2** **NR3C1** **PTPN1**
	Chalcone	Aromatic ketone	$C_{15}H_{12}O$	**ALOX5** **AR** **MAOA** **MAOB**	**ALOX5** CRYZ **MAOA** **MAOB** MAPT MBNL1 MBNL2 MBNL3	**ALOX5** **AR** **MAOB**

					TLR9	
	Coumarin	Benzopyrone	$C_9H_6O_2$	**CA1** **CA2** **CA3** **CA4** **CA5A** **CA5B** **CA12** **CA13** **CA14** **CYP2A6** **MAOA**	**CA1** CA2 CA3 CA4 CA5A CA5B C6 C7 **C9** **CA12** **CA13** **CA14** MBNL1 MBNL2 MBNL3	**CA1** **CA9** **CA12** **CA13** **CA14** CYP2A6 DAO MAOA PGR
Celastrus paniculatus	Paniculatine	Alkaloid	$C_{17}H_{27}NO_2$		ACHE AR **BCHE** DPP4 EBP FAP HSD11B1 HSD11B1L **HSD17B3** HSD17B12 NR3C1 NR3C2 SIGMAR1 SLC6A2 SLC6A3	**HSD17B3** **ACHE** **BCHE**
Nardostachys jatamansi	Valeranone	Sesquiterpene	$C_{15}H_{26}O$		**AR** CA1 CA13 **CA2** CA3 CA5A CA5B CA7 **CES1** **CES2** CES3 CES5A **CYP19A1** MAPT	ALOX5 **AR** **CA2** **CES1** **CES2** **CYP19A1** GPBAR1 HPD

For each bioactive compound, common targets predicted by 2 or more databases are shown in bold

For the bioactive ingredients (Glycyrrhetic acid, Glycyrrhizin, Chalcone and Coumarin) of *Glycyrrhiza glabra*, some protein targets were predicted in common by all the 3 prediction databases. A consensus was observed among the target proteins predicted by at least 2 databases for *Clitoria ternatea, Acorus calamus, Celastrus paniculatus* and *Nardostachys jadamansi*. Different targets were predicted by the 3 databases for *Bacopa monnieri* and *Centella asiatica*. Several of the predicted target proteins have brain-related functions pertinent to their nootropic effects as discussed below.

Plants are a rich source of novel pharmacologically active compounds. To date, >70,000 plant species have been screened for their medicinal use. [8] Drug discovery from plants, driven by bioactivity-dependent fractionation, has led to the discovery of many important drugs. Several of these bioactive ingredients, through a better understanding of their target interactions, mode of action and clinical implications, have found new medical applications. *In silico* analysis of these bioactive compounds are very helpful to establish their mode of action. Our study revealed several potential target proteins involved in neurodevelopmental or neuroprotection processes.

CYP19A1, also known as aromatase which catalyzes the formation of aromatic C18 estrogens from C19 androgens, was predicted to be a target of taraxerol and taraxerone of *C. ternatea*, α asarone and β asarone of

A. calamus, and valeranone of *N. jadamansi*. Estrogen has neurotrophic and neuroprotective effects in the brain. [9] Several genetic and functional lines of evidence support a role of *CYP19A1* in reading, speech and language.[10] A chromosomal translocation in a dyslexic individual was found to disrupt the promoter region of *CYP19A1*.[10] Interestingly, *CYP19A1* gene is located in 15q21 locus, which is also known to harbor *DYX1C1* gene implicated in developmental dyslexia.[11] Moreover, expression of *CYP19A1* was found to be altered in Alzheimer's disease (AD), [12] and several reports suggest a genetic association of *CYP19A1* gene polymorphism with AD. [13,14] Thus, it is an important finding that the bioactive ingredients of the medicinal plants used to enhance cognitive abilities have *CYP19A1* as one of their target proteins.

Microtubule associated protein tau (*MAPT*) was predicted as the target of taraxerone of *C. ternatea*, α asarone and β asarone of *A. calamus,* glycyrrhetic acid and chalcone of *G. glabra,* and valeranone of *N. jadamansi*. Depending on the neuron type and stage of neuronal maturation, the *MAPT* transcripts are differentially expressed in the nervous system. [15] *MAPT* mutations have been associated with several neurodegenerative disorders such as Alzheimer's disease (AD), [16] Parkinson's disease, [17] Pick's disease, [18] frontotemporal dementia, [19] cortico-basal degeneration [20] and progressive supranuclear palsy. [21] Besides, the risk of mild cognitive impairment[22] cognitive decline [23] and memory decline [24] was found to be influenced by genetic variations in *MAPT*.

PTGS1 (COX1) and PTGS2 (COX2) were predicted to be targets of taraxerone of *C. ternatea*, and α asarone and β asarone of *A. calamus.* Several lines of evidence indicate a role of PTGS1 and PTGS2 in the pathogenesis of AD. [25-27] Studies in mice have provided evidence that PTGS1 and PTGS2 have a potential role in learning and memory. [28-30] In fact, inhibition of PTGS1 and PTGS2 has been suggested as a possible therapeutic approach for AD [29] as well as for cognitive impairments. [31,32]

ACHE was predicted as the target of taraxerol (*C. ternatea*) and paniculatine (*C. paniculatus*). Known as a neuromodulator, there is accumulating evidence on the role of acetylcholine in learning and memory. [33,34] In a mouse model of autism, elevation of acetylcholine was found to relieve cognitive rigidity and social deficiency. [35] *SLC6A2* and SLC6A3 were predicted as targets of taraxerol (*C. ternatea*) and paniculatine (*C. paniculatus*). *SLC6A2* and SLC6A3 genes have been reported to be associated with attention deficit hyperactivity disorder in several studies (reviewed by Farone and Mick). [36]

MAOA and MAOB were predicted as targets of α-asarone and β-asarone (*A. calamus*) and chalcone and coumarin (*G. glabra*). Data from humans and animal models suggest that inhibition of MAOA and MAOB lead to cognitive enhancement, which could be used in the treatment of cognitive disorders. [37,38]

Our study to identify the target proteins of bioactive compounds present in Ayurvedic medicinal herbs with nootropic properties has revealed several potential target proteins implicated in neurodevelopment and neuroprotection.

CONCLUSION

The target proteins identified through *in silico* target fishing have been implicated in neurodevelopmental or neuroprotection processes.

Modern approaches to Ayurveda warrant further in-depth drug development efforts, including development of single molecule drugs. This would require vast knowledge on the isolation of a substance in pure form using various separation techniques, its chemical properties and spectral characteristics. Advances in instrumentation and computational methods have now opened up new possibilities for the use of this knowledge in identifying multiple targets, aiding drug development research.

REFERENCES

1. Williams M. Genome-based drug discovery: prioritizing disease-susceptibility/disease-associated genes as novel drug targets for schizophrenia. Curr Opin Invest Drug. 2003; 4(1): 31–36.
2. Bottcher TB, Pitscheider M, Sieber S. Natural products and their biological targets: Proteomic and metabolomic labeling strategies. Angew Chem Int Ed Engl. 2010; 49(15): 2680–2698.
3. Cheng KW, Wong CC, Wang M, He QY, Chen F. Identification and characterization of molecular targets of natural products by mass spectrometry. Mass Spectrom Rev. 2010; 29(1): 126–155.
4. Bagchi P, Kar A. Ayur-Informatics: Establishing an in-silico-ayurvedic medication and RNAi treatment for schizophrenia. J Biosci Tech. 2011; 2(1): 205-212.
5. Mohd Fauzi F, Koutsoukas A, Lowe R, Joshi K, Fan TP, Glen RC, Bender A. Chemogenomics approaches to rationalizing the mode-of-action of traditional Chinese and Ayurvedic medicines. J Chem Inf Model. 2013; 53(3): 661-673.
6. Fauzi FM, Koutsoukas A, Lowe R, Joshi K, Fan TP, Glen RC, Bender A. Linking Ayurveda and Western medicine by integrative analysis. J Ayurveda Integr Med. 2013; 4(2): 117-119.
7. Rao RV, Descamps O, John V, Bredesen DE. Ayurvedic medicinal plants for Alzheimer's disease: a review. Alzheimers Res Ther. 2012; 4(3): 22.
8. Veeresham C. Natural products derived from plants as a source of drugs. J Adv Pharm Technol Res. 2012; 3(4): 200-201.
9. Brann DW, Dhandapani K, Wakade C, Mahesh VB, Khan MM. Neurotrophic and neuroprotective actions of estrogens: Basic mechanisms and clinical implications. Steroids. 2007; 72(5): 381–405.
10. Anthoni H, Sucheston LE, Lewis BA, Tapia-Paez I, Fan X, Zucchelli M, et al. The aromatase gene *CYP19A1*: Several genetic and functional lines of evidence supporting a role in reading, speech and language. Behav Genet. 2012; 42(4): 509–527.
11. Taipale M, Kaminen N, Nopola-Hemmi J, Haltia T, Myllyluoma B, Lyytinen H, et al. A candidate gene for developmental dyslexia encodes a nuclear tetratricopeptide repeat domain protein dynamically regulated in brain. Proc Natl Acad Sci U S A. 2003; 100(20): 11553-11558.

12. Luchetti S, Bossers K, Van de Bilt S, et al. Neurosteroid biosynthetic pathways changes in prefrontal cortex in Alzheimer's disease. Neurobiol Aging. 2011; 32(11): 1964-1976.
13. Chace C, Pang D, Weng C, et al. Variants in CYP17 and CYP19 Cytochrome P450 genes are associated with onset of Alzheimer's disease in women with Down syndrome. J Alzheimers Dis. 2012; 28(3): 601-612.
14. Medway C, Combarros O, Cortina-Borja M, et al. The sex-specific associations of the aromatase gene with Alzheimer's disease and its interaction with IL10 in the Epistasis Project. Eur J Hum Genet. 2014; 22(2): 216-220.
15. Andreadis A. Tau gene alternative splicing: expression patterns, regulation and modulation of function in normal brain and neurodegenerative diseases. Biochim Biophys Acta. 2005; 1739(2-3): 91-103.
16. Rademakers R, Dermaut B, Peeters K, Cruts M, Heutink P, Goate A, Van Broeckhoven C. Tau (MAPT) mutation Arg406Trp presenting clinically with Alzheimer disease does not share a common founder in Western Europe. Hum Mutat. 2003; 22(5): 409-411.
17. Pascale E, Di Battista ME, Rubino A, Purcaro C, Valente M, Fattapposta F, et al. Genetic architecture of MAPT gene region in Parkinson disease subtypes. Front Cell Neurosci. 2016;10: 96.
18. Bronner IF, ter Meulen BC, Azmani A, Severijnen LA, Willemsen R, Kamphorst W, et al. Hereditary Pick's disease with the G272V tau mutation shows predominant three-repeat tau pathology. Brain. 2005; 128(Pt 11): 2645–2653.
19. Rademakers R, Cruts M, van Broeckhoven C. The role of tau (MAPT) in frontotemporal dementia and related tauopathies. Hum Mutat. 2004; 24(4): 277-295.
20. Kouri N, Carlomagno Y, Baker M, Liesinger AM, Caselli RJ, Wszolek ZK, et al. Novel mutation in MAPT exon 13 (p.N410H) causes corticobasal degeneration. Acta Neuropathol. 2014; 127(2): 271–282.
21. Borroni B, Agosti C, Magnani E, Di Luca M, Padovani A. Genetic bases of Progressive Supranuclear Palsy: the MAPT tau disease. Curr Med Chem. 2011; 18(17): 2655-2660.
22. Di Maria E, Cammarata S, Parodi MI, Borghi R, Benussi L, Galli M, et al. The H1 haplotype of the tau gene (MAPT) is associated with mild cognitive impairment. J Alzheimers Dis. 2010; 19(3): 909-914.
23. Goris A, Williams-Gray CH, Clark GR, Foltynie T, Lewis SJ, Brown J, et al. Tau and alpha-synuclein in susceptibility to, and dementia in, Parkinson's disease. Ann Neurol. 2007; 62(2): 145-153.
24. Morley JF, Xie SX, Hurtig HI, Stern MB, Colcher A, Horn S, et al. Genetic influences on cognitive decline in Parkinson's disease. Mov Disord. 2012; 27(4): 512-518.
25. O'Banion MK. COX-2 and Alzheimer's disease: potential roles in inflammation and neurodegeneration. Expert Opin Investig Drugs. 1999; 8(10): 1521-1536.
26. Yermakova AV, Rollins J, Callahan LM, Rogers J, O'Banion MK. Cyclooxygenase-1 in human Alzheimer and control brain: quantitative analysis of expression by microglia and CA3 hippocampal neurons. J Neuropathol Exp Neurol. 1999; 58(11): 1135-1146.
27. Frautschy SA. Thinking outside the box about COX-1 in Alzheimer's disease. Neurobiol Dis. 2010; 38(3): 492-494.
28. Cowley TR, Fahey B, O'Mara SM. COX-2, but not COX-1, activity is necessary for the induction of perforant path long-term potentiation and spatial learning in vivo. Eur J Neurosci. 2008; 27(11): 2999-3008.
29. Choi SH, Aid S, Caracciolo L, Minami SS, Niikura T, Matsuoka Y, Turner RS, Mattson MP, Bosetti F. Cyclooxygenase-1 inhibition reduces amyloid pathology and improves memory deficits in a mouse model of Alzheimer's disease. J Neurochem. 2013; 124(1): 59-68.
30. Shang JL, Cheng Q, Yang WF, Zhang M, Cui Y, Wang YF. Possible roles of COX-1 in learning and memory impairment induced by traumatic brain injury in mice. Braz J Med Biol Res. 2014; 47(12): 1050–1056.
31. Müller N, Riedel M, Schwarz MJ, Engel RR. Clinical effects of COX-2 inhibitors on cognition in schizophrenia. Eur Arch Psychiatry Clin Neurosci. 2005; 255(2): 149-151.
32. Chen R, Zhang J, Fan N, Teng ZQ, Wu Y, Yang H, et al. Δ9-THC-caused synaptic and memory impairments are mediated through COX-2 signaling. Cell. 2013; 155(5): 1154-1165.
33. Hasselmo ME. The role of acetylcholine in learning and memory. Curr Opin Neurobiol. 2006; 16(6): 710-715.
34. Picciotto MR, Higley MJ, Mineur YS. Acetylcholine as a neuromodulator: cholinergic signaling shapes nervous system function and behavior. Neuron. 2012; 76(1): 116–129.
35. Karvat G, Kimchi T. Acetylcholine elevation relieves cognitive rigidity and social deficiency in a mouse model of autism. Neuropsychopharmacology. 2014; 39(4): 831-840.
36. Faraone SV, Mick E. Molecular genetics of attention deficit hyperactivity disorder. Psychiatr Clin North Am. 2010; 33(1): 159-180.
37. Delumeau JC, Bentué-Ferrer D, Gandon JM, Amrein R, Belliard S, Allain H. Monoamine oxidase inhibitors, cognitive functions and neurodegenerative diseases. J Neural Transm Suppl. 1994; 41: 259-266.
38. Cai Z. Monoamine oxidase inhibitors: promising therapeutic agents for Alzheimer's disease (Review). Mol Med Rep. 2014; 9(5): 1533-1541.
39. Pase MP, Kean J, Sarris J, Neale C, Scholey AB, Stough C. The cognitive-enhancing effects of Bacopa monnieri: a systematic review of randomized, controlled human clinical trials. J Altern Complement Med. 2012; 18(7): 647-652.
40. Gohil KJ, Patel JA, Gajjar AK. Pharmacological Review on Centella asiatica: A Potential Herbal Cure-all. Indian J Pharm Sci. 2010; 72(5): 546–556.

41. Margret AA, Begum TN, Parthasarathy S, Suvaithenamudhan S. A Strategy to Employ Clitoria ternatea as a Prospective Brain Drug Confronting Monoamine Oxidase (MAO) Against Neurodegenerative Diseases and Depression. Nat Prod Bioprospect. 2015; 5(6): 293-306.
42. Singhal AK, Naithani V, Bangar OP. Medicinal plants with a potential to treat Alzheimer and associated symptoms. Int J Nutr Pharmacol Neurol Dis. 2012;2(2): 84-91.
43. Cui YM, Ao MZ, Li W, Yu LJ. Effect of glabridin from Glycyrrhiza glabra on learning and memory in mice. Planta Med. 2008; 74(4): 377-380.
44. Bhanumathy M, Harish MS, Shivaprasad HN, Sushma G. Nootropic activity of Celastrus paniculatus seed. Pharm Biol. 2010; 48(3): 324-327.
45. Joshi H, Parle M. Nardostachys jatamansi improves learning and memory in mice. J Med Food. 2006; 9(1): 113-118.
46. Khan MB, Hoda MN, Ishrat T, Ahmad S, Moshahid Khan M, Ahmad A, et al. Neuroprotective efficacy of Nardostachys jatamansi and crocetin in conjunction with selenium in cognitive impairment. Neurol Sci. 2012; 33(5): 1011-1020.

Cite this article as:
Suresh A. Poovathinal, Ayyappan Anitha, Premjith Puliyappatta, Vijitha Viswambharan, Ismail Thanseem. In Silico Target Identification of Nootropic Bioactive Compounds from Ayurvedic Herbs. International Journal of Ayurveda and Pharma Research. 2017;5(4):55-61.
Source of support: Nil, Conflict of interest: None Declared

***Address for correspondence**
Dr. Ayyappan Anitha
Dept. of Neurogenetics
Institute for Communicative and Cognitive Neurosciences (ICCONS)
Kavalappara, Shoranur, Palakkad, Kerala, India.
Tel: +91 466 2223038
Fax: +91 466 2223038
E-mail: anitha.a72@gmail.com