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Mini Review

Acetylcholinesterase inhibition and phyto-constituents

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Plants are the next door neighbors for the people from ancient time, which are used to fulfill daily needs. Most of the population still uses the traditional medicines to cure disease by following their indigenous protocols. Acetylcholine (Ach) is a neurotransmitter, helps in boosting memory and learning. Disturbance in Ach production and release causes fatal disease like Alzheimer and neuro-muscular disorders. Donepezil, Galantamine and other Acetylcholinesterase inhibitor are used to treat them. These drugs prevents rapid hydrolysis of Acetylcholine by antagonize the action of Acetylcholinesterase. Now a day's most of the research is being carried on natural source. Numerous phyto- constituents are under clinical trial to validate its potential scientifically. Plants and phyto- chemicals are assessed to potentiate the acetylcholine production and delay its hydrolysis. This communication is only to provide the list of plants and their phyto- constituents which antagonize the Acetylcholinesterase action. It consists of plant and their Phyto- constituents which are tested in last 7 years with IC_{50} value.

Keywords- Alzheimer's disease, Folklore, Phyto- constituents, Neuromuscular transmission

Traditional medicines are used by all civilization in the world, since time immemorial. Herbal drugs cure the disease in a holistic approach with natural harmony. About 70–95% people of developing countries are still using traditional medicines for their health care needs at primary level (Anonymous.2013). Traditional systems of medicines are basically originated from plants. Because, plants are easily available, having low cost and believe to be much effective with fewer side effects. In year 2008, global market of herbal medicines was 83 billion US $ (Randhava, 2013) and may be increased up to 107 billion US$ in 2016 (http://www.companiesandmarkets.com/). About 25 % of modern medicines are derived from natural origin (Randhava, 2013). Tradition based knowledge is a basic background to initiate, analyze and discover new treatments of disease for human well being with a modern scientific approach. Only 10-15 % of plants have been explored from total vegetation which is used in modern pharmaceutical sciences (Saklani and Kutty, 2008). Acetylcholine (Ach) is a neurotransmitter synthesized in nerve terminals; plays an important role in memory, recognition and increase synaptic transmission in neuromuscular junction (Blokland, 1996). Acetylcholinesterase (AChE) is an enzyme of serine family which trigger the rapid hydrolysis of acetylcholine into acetate and choline molecule (Mukherjee et al., 2007). With advance age impairment in Ach synthesis, activation its release and hydrolysis is common and results in loss of memory and disturbance in neuromuscular transmission (Mouisel et al., 2006). It occurs due to lesions in cholinergic nuclei and anatomical changes in cholinergic pathway (Winkler et al., 1995) and results in memory loss (Everitt et al., 1997, Ikarashi et al., 2004), impaired visuo-spatial tasks and verbal test (Kopelman et al., 1988). Ach help in encoding new information in the hippocampus (Hasselmo, 1999), and enhance memory in patients of dementia. Selective suppression of acetylcholine in synapse causes loss of previously learned work or other things (Hironaka et al., 2001). Acetylcholinesterase inhibitors increase the concentration of acetylcholine, and increase synaptic transmission between neurons. Release of Ach and delay in hydrolysis is only the treatment for Alzheimer's and other neurodegenerative diseases (Rasool et al., 2014, Baruah et al., 2008). In last 20 years numerous medicines are clinically assessed which antagonize the AChE activity and employed to treat neurodegenerative disease (Anand et al., 2014). Various plant extracts and phyto- constituents have the ability to antagonize the activity of acetylcholinesterase, such as Physostigmine, Galantamine, Huperzine A, and Curcumin (Huang et al., 2013). These drugs have a promising effect in the management of myasthenia gravis, glaucoma, and Alzheimer's disease (Lu et al., 2011). In last decay various studies has been conducted on plants to analyze the effect on neurodegenerative disease. This review consists of phyto – constituent's possessing AChE inhibitory potential which are analyzed between years 2007-2014 by conducting literature survey in scientific database such as Science direct, Pubmed central and Google scholar. Phyto- constituents are listed with IC_{50} value and their botanical source **(Table 1).** In last century various traditional medicines are validated scientifically according to their traditional use. In recent times, on the basis of traditional uses; numerous phyto- pharmaceutical are under clinical and post clinical study to validate its potential. Now, a day huge financial support has been provided to by govt. and pharmaceutical firms to improve and rediscover the tradition based scientific studies. According to WHO report, research oriented program has been growing 5% annually in Brazil, China, India (Anonymous, 2013). About 100 plant derived medicines and at least 100 phyto-chemicals are undergoing in clinical and preclinical development stage of drug discovery respectively (Harvey, 2008). It is necessary to develop our traditional folklore knowledge on the basis of scientific data. To develop phyto- pharmaceutical as a first choice treatment, needs a financial support and well trained professional. It will be done only by the union of govt. and pharmaceuticals firms, which foster the research on natural resources for the well being of mankind.

It will be completed by taking clinical trials on herbal medicines will be conducted globally to provide, its safety and efficacy. These phyto-chemicals will be further investigated to deliver best results by making its formulation.

Table 1. Phyto-constituents responsible for AChE inhibition

S.N	Name of Plant (Family)	Phytoconstuients (IC_{50} value)	Refrence
1.	Abuta grandifolia (Mart.) (Menispermaceae)	(R, S) – 2 N- norberbamine.	Commet et al., 2012.
2.	*Acacia cyanophylla* Lindl (Fabaceae)	Isosalipurposide 1, 52.04 µg/mL.	Ghribia et al., 2014.
3.	*Alpiniae officinarum* Hance (Zingiberaceae)	Galangin (120 µM/ml)	Guo et al., 2010.
4.	*Alstonia macrophylla* Wall. ex G. Don. (Apocynaceae)	Naresuanoside.	Changwichit et al., 2011.
5.	*Anemarrhena asphodeloides* AA (Liliaceae)	Timosaponin AIII (35.4 µM/ml).	Lee et al., 2009.
6.	*Angelica gigas* Nakai (AGN) (Apiaceae)	Nodakenin (84.7 µM/ml).	Kim et al., 2007.
7.	*Angelica archangelica* L. (Apiaceae)	Heraclenol-2'-O-angelate (14.4±3.2 µM).	Wszelaki et al., 2011.
8.	*Betula platyphylla* Suk. (Betulaceae)	Aceroside VIII , platyphylloside.	Lee et al., 2012.
9.	*Buddleja asiatica* Loureiro, Fl. Cochinch (Buddlejaceae)	Asiatoates A (5.54 µM/ml) &B (8.34 µM/ml).	Ali et al., 2013.
10.	*Capsosiphon fulvescens* Setchell & N.L (Ulotrichaceae)	Capsofulvesins A-C(50. 90 to 82.83µM/ml).	Fang et al., 2012.
11.	*Cassia obtusifolia* Linn (Caesalpiniaceae)	Gluco-obtusifolin (37.2µM/ml)	Kim et al., 2009.
12.	*Catharanthus roseus* (Apocynaceae)	Serpentine (0.775 µM/ml)	Pereira et al., 2010.
13.	*Centella asiatica* (L.) (Umbelliferae)	Asiatic acid (14µM/ml)	Nasir et al., 2010.
14.	*Citrus hystrix*. DC (Rutaceae)	Isoimparatorin(23±0.2µM/ ml)	Youkwan et al., 2010.
15.	*Cnestis ferruginea* Vahl ex DC (Connaraceae)	Amentoflavone.	Ishola et al., 2013.
16.	*Commiphora whighitii* (Arn.) Bhandari SCN (Burseraceae)	Gugulipid.	Saxena et al., 2007.
17.	*Crocus sativus* L. (Iridaceae)	Crocins.	Pitsikas et al., 2007.
18.	*Ervatamia hainanensis* Tsiang (Apocynaceae)	Coronaridine, voacangine.	Zan et al., 2010.
19.	*Garcinia hombroniana* Pierre bark (Clusiaceae)	2*β*-hydroxy-3*a*-*O* caffeoyltaraxar-14-en-28-oic acid.	Jamila et al., 2014.
20.	*Habranthus jamesonii* (Baker) Ravenna (Amaryllidaceae)	Sanguinine (0.7 µg/mL)	Cavallaro et al., 2014.
21.	*Himatanthus lancifolius* Seidl C, Correia BL, Stinghen AE (Apocynaceae)	Uleine (0.45 µM/ml)	Seidl et al., 2010.
22.	*Hippeastrum vittatum* (L'Hér.) (Liliaceae)	Montanine.	Pagliosa et al., 2010.
23.	*Holarrhena antidysenterica* (Linn.)Wall. (Apocynaceae)	Conessimin(4 µM/ml)	Yang et al., 2012.
24.	*Hopea chinensis* Hand. -Mazz. (Dipterocarpaceae)	Hopeachinols & hopeachinols C(4.81 & 11.71 µM/ml).	Yan et al., 2012.
25.	*Hopea hainanensis* Merr. & Chun(Dipterocarpaceae)	Hopeahainol A (4.33 µM/ml).	Ge et al., 2008.

26.	*Hypericum cohaerens* N. Robson (Hypericaceae)	Hypercohins B-D (5.8-17.9 µM/ml)	Liu et al., 2013.
27.	*Illicium simonsii* Maxim (Illiciaceae)	Clovanedunnianol.	Dong et al., 2013.
28.	*Knema laurina* Warb (Myristicaceae)	2-hydroxy-6-(10'(Z)heptadecenyl) benzoic(0.573 ± 0.0260 µM/ml)	Akhtar et al., 2011.
29.	*Lobelia laxiflora* L.(Campanulaceae)	N-methyl-2(2'-methoxybutyl), 6(2''-hydroxybutyl)-3-piperidine.	Enas et al., 2014.
30.	*Lycopodiastrum casuarinoides* (Spring) Holub (Lycopodiaceae)	Casuarinines C.	Tang et al., 2013.
31.	*Macaranga kurzii Pax &K.Hoffm.*(Euphorbiaceae)	Trans-3,5-dimethoxystilbene(9 µM/ml).	Thanh et al., 2012.
32.	*Magnolia officinalis* Rehder & E.H.Wilson (Magnoliaceae)	Magnolol.	Le et al., 2013.
33.	*Mesua elegans* (King) Kosterm. (Clusiaceae).	Mesuagenin B (0.7 µM/ml).	Awang et al., 2010.
34.	*Morus lhou* Linn (Moraceae)	Morusinol(3.1 µM/ml)	Kim et al., 2011.
35.	*Murraya koenigii* (L.) Sprengel (Rutaceae)	Mahanimbine (0.03 mg/mL)	Kumar et al., 2010.
36.	*Murraya paniculata* (L.) Jack (Rutaceae)	Euchrestifoline(93.1 µM/ml)	Rehman et al., 2013.
37.	*Nelumbo nucifera* Gaertn. (Nelumbonaceae)	Procyanidins.	Xu et al., 2009.
38.	*Panax ginseng* C.A. Meyer (Araliaceae)	Ginsenoside Rb1.	Kim et al., 2013.
39.	*Polygala tenuifolia* (Yuan Zhi) (Polygalaceae)	Tenuifolin.	Zhang et al., 2008.
40.	*Polygala molluginifolia* A. St.-Hil. and Moq (Polygalaceae)	Isoflavones 2-4 (84 µmol /L).	Venzke et al., 2013.
41.	*Poncirus trifoliata* Rafin.(Rutaceae)	Methoxsalen.	Kim at al., 2011.
42.	*Psoraleae corylifolia Linn* (Leguminosae)	Psoralen.	Wu et al., 2007.
43.	*Schizandra chinesis* Baill Schisandraceae	Schizandrin.	Giridharan et al., 2012.
44.	*Stemona sessilifolia* Bai Bu (Stemonaceae)	Stenine B (2.1±0.2 µM/ml).	Lai et al., 2012.
45.	*Stephania rotunda* (Muell. Arg.) Woodson (Menispermaceae)	Stepharotudine.	Hung et al., 2010.
46.	*Tabernaemontana divaricata* (L.) R.Br. (Apocynaceae)	3'-R/S-hydroxyvoacamine (7.00±1.99 µM/ml).	Chaiyana et al., 2013.
47.	*Terminalia chebula* Retz. (Combretaceae)	1,2,3,4,6-penta-O-galloyl-β-d-glucose.	Sanchetia et al., 2013.
48.	*Triclisia sacleuxii* (Pierre) Diels. (Menispermaceae	Lindoldhamine(50 µM/ml).	Murebwayire et al., 2009.

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