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Combating attention deficit hyperactivity disorder with natural treatment

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Attention deficit hyperactivity disorder (ADHD) is a weakening mental health problem that hampers the child development. Both the hereditary and ecological elements are the primary causes behind the challenge and possibly will be different among persons. The drugs are used for ADHD may be enhancing the health problem. Therefore, huge requirement of ayurvedic based foodstuff is anticipated among the end users that are expected to be healthy as well as afford additional functional benefits. An ayurvedic plant such as brahmi (*Bacopamonnieri* and *Centellaasiatica)* is reported to have much useful functional benefits. Brahmi is well-known to harness reminiscence, perception, being sensible and further mental disorderliness. The present review enlightens the functional properties of brahmi for children with ADHD, including intervention programme.

Keywords: ADHD, Ayurvedic plant, Health benefits, Intervention programme

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Mental disorder is now foremost thing a cause of disability in childhood[1]. Attention deficit hyperactivity disorder (ADHD) is an unbearable mental confusion that slows down the children's growth[2]. It is among the commonest childhood stage neurobehavioral disorderliness and is known to intensely impact the scholastic performance, happiness and communal relationship of kids[3]. ADHD portray by persistent sign such as inattention, hyperactivity and impulsivity[4]. It has a universal occurrence with an estimated 6% incidence[5] and is commonly identified in the age group of 2-7 years that is in preschool aged children.[6]

As stated by World Health Organization (WHO), a cerebral disarray are to amplify by 50% in the year of two thousand and twenty, is the fore most finding root of morbidity in kids. The kids represent on 40% in India and the rate of psychopathology amid childhood is 5 to 15%. A recent analysis estimated that the global cumulative impact of mental disorder in terms of economic output will amount to US$ 1600 billion over next 20 year.[7]

Numerous research have stated greatly variable rates of ADHD around the world, starting from as low as 1% to as high as almost 20% among school children[8,9] and its noticeable in the ages of 6 and 12 years[10]. The occurrence rate of ADHD in United State of America is 4 to 8%[11], In Korea it is noticed to be 7.6% to 9.5%[12] and 10 to 20% in India[13] and 1 to 17.7% in India[14]. The issue of ADHD disorder is a major threat among primary school children[15], but continues into adulthood too[16].

The occurrence of ADHD between boys and girls differ around the world and the ratio ranged from 2:1 to 6:1. The majority studies noticed that boys are more affected with ADHD than the girls[17]. In favor of above findings, USA reported a 3.62% of boys and 0.85% of girls faced ADHD out of 10,438 children who were assessed for the study[18]. A similar finding noticed in Colombia too, reported the occurrence in boys (19.8%) than girls (12.3%)[19]. The gender disparity in ADHD are more, this may be because of the girls with neurobehavioral disorder are undiagnosed[20,21].

The hereditary and the atmospheric surrounding are fore most position in etiology of ADHD and earlier research findings revealed about ADHD amongst identical twins (8%), fraternal twins (32%) and first-degree relatives (25%). Environmental consequence such as maternal stress and smoking habit among family members during pregnancy, poor quality early care giving, prenatal complications and prematurity also plays a leading part.

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The dimension of the brain construction for ADHD affected pupil is reduced roughly 5 to 10% and magnetic renounce imaging screened reduced blood level in striatum and shortage in functional networks[22]. The ADHD prime uniqueness are lack of concentration, tendency to act on a whim and restless and these personality will lead to lack of communal bond, acquisition of knowledge in the school and disturb other person as well[23]. The secondary personalities are difficulty to create bond with the peer group. In that case, this kind of personality kids may keep away from peer group and communal pupil[24,25].

The synthetic food additive, colours and chemical (salicylates) will enhance the restlessness[26,27] and these findings tested by Stevens[28]. Appropriate diet is needed for kids and kids like to eat more of junk food and they face hyperactivity, this may reflect a long-term nutritional imbalance[29]. Thus, advice to parents to polished grains, only energy rich foodstuff, sweets and preserved foodstuff, synthetic additives and colours must be avoided entirely from the foodstuff.

Drugs are used in ADHD are psycho stimulants, tricyclic antidepressants and tranquilizers. These drugs may be enhancing the possibility of heart related problem, liver injury and other health issue[30]. Today the need came to find out effective treatment without hampering the development of health and psychology of children. Therefore, actual need of our natural medicine and several traditional based food products. In that case, the need for exploration of new foodstuff from naturally available source may enhance the cognition ability and earlier studies noticed that the ayurvedic plant such as *Bacopamonnieri (BA) and Centellaasiacitica (CA)* has potency to increase the mental function.

Health benefits of ayurvedic plants

Ayurveda, which is more than 5 thousand years older and it has a beneficial effect on nerve function (CNS) and increase the mental capability[31,32,33]. Nootropic plants are used to increase mental function, example of ayurvedic plant with nootropic activity such as *Ginkgo biloba, B. monnieri, C. asiatica. Withaniasomnifera and Convolvulus Pluricaulis.* The bramhi *(C. asiatica. B.monnieri)* which contain large amount of secondary metabolites providing active compounds stimulating cell upgrading, enhancephysical and mental health. Both plants (*Bacopamonnieri* and *Centellaasiatica*) possess neuroprotective properties, neurotropic action with beneficial application[33].

Bacopamonnieri

Bacopa called brahmi includes 46 species, water in habitat and are found in hot zone of the globe including India, Nepal, Sri Lanka, China, Taiwan and Vietnam and parts of USA[34]. In India, it is found in soggy, muddy spot and grows well on the banks of unhurried flowing rivers and lakes upto an attitude of 1,320 m. It is a small climber, fastly spreads and have succulent parts and has abundant branches and small fleshy, oblong leaves. Flowers and fruits appear in summer and the entire plant is medicinally important[35,36].

The group of plant therapeutic called *medhyarasayana* are well-known to boost mental health, intellect and memory (medhya) and are believed to prop up longevity and rejuvenation (rasayana)[37]. The brain, being the creative centre of humans[35] is expected to be influenced by the brahmi as sanskrit name brahmi stems from Brahma-the creative aspect of God. *B. monnieri* is recognized for use over centuries as a brain tonic, memory enhancer, revitalize sensory organs. It is also further used as a medicine inanti-anxiety, as a cardio-tonic, diuretic, antidepressant and anticonvulsant agent[36]. It is very effectively used as an anti inflammatory, analgesic, antipyretic, epilepsy, anticancer therapeutics and is a good antioxidant[38,39]. Skin ailments such as eczema, psoriasis, abscess, ulcerations and leprosy are treated with the products made out of *Bacopa* in India and Pakistan. Further, it is also useful in treatment of chronic rheumatism as an ointment and to treat asthma and hoarseness in voice[40].

The Bacopa has a high moisture content (88%), carbohydrate (5.9%), fat (0.6%) and protein (2.1%). Plant secondary metabolites such as phenylethanoid glycosides, flavonoids, amino acids such as alpha-alanine, aspartic acid, glutamic acid and betulinic acid, stigmasterol, b-sitosterol and stigmastrenol are registered in these plants[41,42,35].

The bioactive composites (bacoside A&B) and amino acids in these ayurvedic are increase the protein kinase action to produce protein and these protein may repair the damaged neurons[43,44,45]. The numerous study noticed that two main saponin (Bacoside A&B) enhance the learning ability in rats[46,44,47,36]. In adding up, bacoside A fraction is more faster than the bacoside B fraction[48] and it plays foremost position to increase positive effect on mental function[49] and this bioactive compound have antidepressant property as well[50].

Various study revealed that the presence of different tetra cyclic triterpenoid saponin is accelerating the cognition activity[51,52]. Numerous studies concluded that the bacosides are reported as a scavenger of free radicals[53,54,55,56].

The defensive reactions of the *Bacopa* plant extort on brain mitochondrial enzyme action in rats were well documented in previous studies[57]. The reaction of *B. monnieri* extort on the cognition performance while ageing was well documented[58,59] and has a task in ayurvedic therapies for treating cognitive disorderliness during aging[60]. Studies on animal version has depicted their role in escalating memory competence and be with neuroprotectant action against Alzheimer's disease[61,62]. *Bacopamonnieri* extract in the quantity of 300 mg/day for 6 weeks of administration on a group of people, the experiment exposed that the increasing technical evidence supporting the cognitive improvement effects[63]. In a study to treat aluminium induced oxidative stress, the neuro protective reaction of the *B. monnieri* in the hippocampus part of rat brain well evidently documented[64]. The extracts of *B. monnieri give* relief to patients affected with anxiety or epileptic disorders[65,66,67,68]. Epilepsy and hysteria is treated with medicated ghee from *B. monnieri*[69].

Sentence repetition and logical reminiscence were found to be dramatically improved in children who took *Bacopa*[70]. In yet another study use of *Bacopa* on children for 42 days, was exposed to boost the mean auditory and visualnotably.[71]

Centella Asiatica

Centellaasiatica L. (Gotu Kola) is a tropical medicinal plant and grows in India, China, Indonesia, Malaysia, Sri Lanka South Africa and Madagascar[72]. It is a nerve tonic and micronutrient in the plant extort was found to be accountable to retard brain aging and also assisted replenishment of neural tissue. Thus was believed to boost reminiscence and invigoratethe brain as well beyond increasing the attention span and concentration[73]. As an ayurvedic agent was used forcuring skin related troubles, laceration and rejuvenating the brain function[74,75].

C. asiatica has a wider health benefits and therefore, its use in food processing is found increasing over the years. It is registered in medicinal use as a potential antioxidant, known for antimicrobial, cytotoxic, neuroprotective properties as well and other activities too. It possesses bioactive constituents viz., triterpenic acid (asiatic acid madecassoside acid), triterpenic saponin (madecassoside and asiaticoside), flavonoids and further phenolic compounds[76,77,78]. The asiaticoside is the most plentiful triterpene glycoside, which, it enhance the antioxidant level in wound healing process[79].

Centella contains nearly eighty eight per cent of moisture, three hundred and ninety one milligram of potassium and one hundred and seventy one milligram of calcium (low in protein, carbohydrate and fat content). The brahmic acid, isobrahmic acid, brahminoside, and brahmoside present in *C. asiatica* have shown some psychotropic, sedative and anticonvulsant factors. It is useful to treat dementia, brain associated disorderliness and anxiety[80].

C. *asiatica* has been found to be efficient in opposition to diabetes mellitus[81], depression[82], wound-healing activity, antibacterial activity[83], neuroprotective activity[84]. The intake of *C. asiatica* is useful to prevent oxidative damage. As a powerful antioxidant, it used as an important neuroprotective effect and provide protection to the rat's brain for age-related oxidative damage[85,86,87]. The components in the ayurvedicis useful for enhancing renovate of injured neurons through hasten nerve regeneration[84,88]. Asiaticoside and brahmoside are found to hold anxiolytic activity through inhibition of phospholipase action in rat cerebellum[89].

The median lethal dose of dried powder of *C. asiatica*, given as an oral dose to mice, was found to be higher than 8 g/kg[90]. Further, Wistar rats (both sex) that received different doses of *C. asiatica at* 20, 200, 600 and 1200 mg/kg/day for six months, let out no symptoms of important changes of body mass and blood analysis in comparison to control group[91].

Measure of medhyarasayana

Bacopa can be taken in the form of non-standardized powder (5-10 g), mixture (8-16 mL), and syrup (30 mL) in each day[92]. Dosages of a 1:2 solution extort are in the range of 5-12 mL/day for adults whereas it was 2.5-6 mL/ day for kids ages 6-12[93]. A *Bacopa* syrup preparation, equal to 1 g dehydrated *Bacopa* leaf at the daily basis for 3 months among 40 children in the ages of 6–8 years, showed strengthening, reminiscence perception and response performance and no side effects were reported[94]. Fifty four people (65 years) administrated 300 mg of *Bacopamonnieri* extract for twelve weeks and none of the participants had any sign of dementia or severe memory loss[95]. A an additional study, researchers gave participants aged 55 and above (person with

memory loss) 125 mg/day of *Bacopamonnieri* extract for 12 weeks, noticeably better mental control, logical memory function, and paired association learning[96].

A usual each day quantity of C. *asiatica* approximately at 600 mg of dehydrated leaf or mixture, single-dose tablet, a 10-mg strong extort accessible in the form of tablet was found very effective[97]. Dehydrated leaves as a tea, by addition of 5-10 g in bubbling hot water (150 mL) and allowed to sheer for 15 min and 3 cups /day was advisable. The systemized Centella extort have up to 100% total saponins (triterpenoids), 60 mg of extort 1 or 2/day, are regularly utilized in recent herbaceous medication. A few side effects such as skin allergy and burning sensations (with external use), headache, stomach upset, nausea, dizziness and drowsiness were reported, however, for a recommended dose no known toxicity was found[98,99].

ADHD interventions

ADHD is more occurrences in primary school going children and it's throughout the lifelong problems. This is the right time to give intervention programme to ADHD affected children. Teacher should know more about the ADHD than their parents, as they intermingle with kids for a more time than parent[100].

The educational intervention is to promote normal behavior and plan to enhance the school performance through improvement in education, concentration power, memory and behavior. The foremost thing of school intervention is to increase positive education outcome[100]. To strong the above evidence, educational intervention are effective to increase mental function amid children[101]. It is not control the behavior but improving habits and day to day activities which enhance the leaning power[24]. Moreover the intervention is based on atmosphere surroundings and mental ability to learn[102]

ADHD is often treated with clinical interventions and behavioural interventions. Treatments for kids with ADHD may harmfully impact upon both communal and education performance[103]. The study argued that drug again and again, only helps aggravate 'symptoms', but do not help the youngster to task efficiently in academic level and it will lead to severe side effects with drug[104]. Thus, educational interventions consider as more desirable and effective strategies to treat ADHD disorder affected children[105].

ADHD in India, limited awareness is reported in the survey[13,106]. According to Wilcox, much families with ADHD either unknowing of the situation or unsure of the suffering itself[107]. A tiny concordance amid parents and teachers in acknowledgement ADHD may be a major reason behind these scenarios. A need is therefore to augment much research on ADHD in India[108].

Discussion

Studies on different clinical and experimental trial reported that the ayurvedic plant has properties of nootropic, cognition enhancing, learning and neuroprotective properties. Bacopa posses the most enhancing capabilities to improve the mental ability, induce cognition function and positively modify behavior by increased level of serotonin and other neurotransmitters. *Centella* has property of increasing the learning capacity by induce dendriticarborization in amygdaloidal nucleus. There is positive result in clinical and experimental about *bacopa* and *centella* on ADHD. However, it's a natural product, the challenge is to describe the mechanisms and paths intricate in the nootropic and retention improving roles stimulus by brahmi. The specific compounds from BM and CA such as bacosides, asiaticoside and asiatic acid are the revitalizing properties. In the field of the therapeutics, has been a continuous discrepancy amongst scientists using clean composites and persons using natural extracts. Hence, the upcoming of investigation in brahmi will be focus to molecular investigation of the properties of different composites vs natural extracts in interpolation bio assay effects and its health benefits.

Conclusion

Ayurvedic plant could deliver a flawless response to ADHD affected kids with harmless to health. *Bacopamonniera Linn. (Brahmi) & Centellaasiatica Linn. (Mandookparni)* is evidenced to control inattention and hyperactivity and thus pave way to further research to set up in a scientific manner.

References

1 Castello EJ, Costello AJ, Edelbrock KC, Burns BJJ, Dulcan MK and Brent D, Psychiatric disorder in pediatric primary care: prevalence and risk factors, Archives of general psychiatry, 45 (1998)1107-1116.

2 American Psychiatric Association, Diagnostic and statistical manual of mental disorders, 4theditin, Text revision, Washington, DC: American Psychiatric Association (2000).

3 American Academy of Pediatrics (AAP), ADHD: clinical practice guideline for the diagnosis, evaluation and treatment of attention deficit hyperactivity disorder in children and adolescents, Pediatrics, 128 (2011)1007-1022.

4 Mosby, Medical Dictionary, 8th ed, Philadelphia, PA: Elsevier, (2009).

5 Polanczyk GV, Willcutt EG, Salum GA, Kieling C and Rohde LA, ADHD prevalence estimates across three decades: an updated systematic review and meta-regression analysis, Int J Epidemiol , 43(2) (2014) 434–42.

6 Tripathi N, Ramanjaneyulu, Tiwari B and Krishnaih,. An ayurvedic management of manasavikara with respect to adhd in children, Ayurpharm Int J AyurAlli Sci., 6(1) (2017) 8 – 14

7 The Global Economic burden of non-communicable diseases, World economic forum, Geneva,(2011)

8 Bird HR, The diagnostic classification, epidemiology and cross-cultural validity of ADHD. In: Jensen PS, Cooper JR, Civic Research Institute, eds. Attention Deficit Hyperactivity Disorder: State of the Science: Best Practices. Civic Research Institute, Inc, (2002).

9 Swanson JM, McBurnett K, Wigal T, Pfiffner LJ and Lerner MA, Effect of stimulant medication on children with ADD: A Review of Reviews. Exceptional Children, 60 (1993) 154–162.

10 Brown RT, Freeman WS, Perrin JM, Stein MT, Amler RW and Feldman HM, Prevalence and assessment of Attention-Deficit/Hyperactivity Disorder in primary care settings, Pediatrics, 107(3) (2001)1-11.

11 Subcommittee on Attention-Deficit/Hyperactivity Disorder and Committee on Quality Improvement, Clinical Practice Guideline: Treatment of the school-aged child with attention-deficit/hyperactivity disorder, Pediatrics, 108 (2001) 1033-44.

12 Chae PK, Jung HO and Noh K, Attention deficit hyperactivity disorder in Korean juvenile delinquents, Adolescence, 36(144) (2001) 707-25.

13 Malhi P & Singhi P, Spectrum of attention deficit hyperactivity disorders in children among referrals to psychology services', Indian Pediatrics, 37 (11) (2000) 1256-60.

14 Bhatia M, Chaudhary S & Sidana A, Attention Deficit Hyperactivity Disorder among Psychiatric Outpatients, Indian Pediatrics, 36 (6) (1999)583-587.

15 Mukhopadhyay M, Misra S, Mitra T & Niyogi P, 2003. Attention deficit hyperactivity disorder', Indian Journal of Pediatrics, 70 (9) (2003) 789-792.

16 Singeri R, Rajkumar P, Muralidharan K, Chandrashekar R & Benegal V, The association between attention-deficit/ hyperactivity disorder and early onset alcohol dependence: a retrospective study', Indian Journal of Psychiatry, 50 (4) (2008)262-5.

17 Littman E, ADHD Under-diagnosed in Girls', Family Practice News, (2009).

18 Ford T, Goodman R, & Howard M, 2003. The British child and adolescent mental health survey 1999: the prevalence of DSM-IV disorders', Journal of the American Academy of Child and Adolescent Psychiatry, 42 (10) (2003) 1203- 1211.

19 Pineda D, Lopera F, Palacio J, Ramirez D & Henao G, Prevalence estimations of attention-deficit/hyperactivity disorder: differential diagnoses and comorbidities in a Colombian sample', International Journal of Neuroscience, 113 (1) (2003)49-71.

20 Quinn P & Nadeau G, Gender Issues and AD/HD: Research, Diagnosis, and Treatment, Maryland: Advantage Books, (2002).

21 Hinshaw S, Preadolescent girls with attention deficit/ hyperactivity disorder: Background characteristics, comorbidity, cognitive and social functioning and parenting practices', Journal of Consulting and Clinical Psychology, 70 (2002) 1086-1098.

22 Kliegman RM, Stanton, BF, Joseph St. Geme and Schor NF, Nelson Test book of Pediatrics, 20th ed, (2016) 304.

23 Bulut S, Understanding Attention Deficit Hyperactivity Disorder, Baltic Journal of Special Education, 2 (17) (2007) 82-91.

24 Cooper P and Ideus K, Attention Deficit/ Hyperactivity Disorder, A Practical Guide for Teachers. London: David Fulton, (1996)

25 Hinshaw S, & Melnick S, Peer relationships in boys with attention deficit hyperactivity disorder with and without comorbid aggression, Development and Psychopathology, 7 (1995) 627-647.

26 Feingold BF, Hyperkinesis and learning disabilities linked to artificial food flavors and colors, Am J Nurs,75(5) (1975) 797–803.

27 Wender EH, The food additive-free diet in the treatment of behavior disorders: a review, J Dev Behav Pediatr, 7(1) (1986) 35–42.

28 Stevens L, Kuczek T, Burgess JR, Hurt EA and Arnold LE, Dietary sensitivities and ADHD: 35 years of research, ClinPediatr, 50(2011) 279–293.

29 Wiles NJ, Northstone K, Emmett P and Lewis G, Junk food" diet and childhood behavioural problems: results from the ALSPAC cohort, Eur J ClinNutr, (63) (2009) 491-498.

30 Behsnanh RE, Robert MK, Jenson HB, Nelson, Textbook of Pediatrics, editors. 19th ed, Philadelphia, PA: Elsevier Publication, Psychological treatment in children, (2011) 108.

31 Chandrika, UG and Kumara AASP, *Centellaasiatica*: Nutritional Properties and Plausible Health Benefits, Advances in Food and Nutrition Research, 76 (2015) 126-153, ISSN 1043-4526..

32 Tohda C, Kuboyama T and Komatsu K, Search for natural products related to regeneration of the neuronal network. Neuro signals, 14 (2005) 34–45.

33 Shinomol GK, Muralidhara and Bharath MMS, Exploring the role of "Brahmi" (Bocopa monnieri and *Centella asiatica)* in brain function and therapy. Recent Patents on Endocrine, Metabolic & Immune Drug Discovery, 5 (2011) 33–49

34 Barrett SC and Strother JL, Taxonomy and natural history of *Bacopa* (Scrophulariaceae) in California. Systematic Botany, (3) (1978) 408–419.

35 Russo A and Borrelli F, *Bacopamonniera*, a reputed nootropic plant: An overview. Phytomedicine, (12) (2005) 305–317.

36 Chopra RN, Nayar SL, Chopra IC, Glossary of Indian Medicinal Plants. Council of Scientific and Industrial Research: New Delhi, (1956).

37 Singh RH and Singh RL, Studies on the antioxidant anxiety effect of the Medhay Rasayan drug Brahmi (*Bacopa* Monnierilinn) part II (experimental studies), J Res Ind Med Yoga Homeo, (14) (1980) 1-6.

38 Tripathi YB, Chaurasia S, Tripathi E, Upadhyay A and Dubey GP, *Bacopamonniera Linn.* as anantioxidant: mechanism of action, Ind J Exp Biol., 34 (1996)523-526.

39 Sinha S and Saxena R, Effect of iron on lipid peroxidation, and enzymatic and non-enzymatic antioxidants and bacoside-A content in medicinal plant *Bacopamonnieri L.* Chemosphere, 62(8) (2006) 340-50.

40 Shakoor A, Akram A, Ashraf CM and Siddiqui MR, Pharmocognostic study and chemical/pharmacological evaluation of Brahmi –buti, Hamdard Medicus, 37 (1994) 92-109.

41 Chatterji N, Rastogi RP and Dhar ML, Chemical examination of *Baco* pamonniera Wettst.: Part I - Isolation of chemical constituents, Indian J. Chem., 1(1963) 212-215.

42 Jain PD and Kulshreshtha K, Bacoside A_1, A minor saponin from *Bacopamonniera,* The international journal for plant Phytochemistry33(2) (1993) 449-451.

43 Singh HK and Dhawan BN, Effect of *Bacopamonnieri Linn* (Brahmi) extract on avoidance responses in rat, Jethnopharmacol, 5(2) (1982) 205-14.

44 Singh HK and Dhawan BN, Neuropsychopharmacological effects of the ayurvedic nootropic *bacopamonniera Linn.*(Brahmi), Indian J. Pharmacol, (29) (1997) S359–S365

45 Rastogi S, Pal R, Kulshreshtha DK, Bacoside A3A triterpenoidsaponin from *Bacopamonniera,* Phytochemistry, 36(1) (1994) 133-7·

46 Singh HK and Rastogi RP, Srimal RC and Dhawan BN, Effect of bacosides A and B on avoidance responses in rats, Phytother. Res, (2) (1988)70–75.

47 Dey C, 1976. Effect of some centrally active phyto products on maze-learning of albino rats, Indian J Physiol Allied Sci, 30 (1976) 88.

48 Sivaramakrishna C, Rao CV, Trimurtulu G, Vanisree M and Subbaraju GV, Triterpenoid glycosides from *Bacopamonnieri*. Phytochemistry, (66),(2005) 2719-28.

49 Chatterji N, Rastogi RP, and Dhar ML, Chemical examination of *Bacopamonniera Wettst*.: parti-isolation of chemical constituents, Indian J. Chem, 3(1965) 24-29.

50 Zhou Y, Shen YH, Zhang C, Su J, Liu RH and Zhang WD, Triterpenesaponins from *Bacopamonnieri* and their antidepressant effects in two mice models, J Nat Prod., 70(4) (2007) 652-5.

51 Aithal HN and Sirsi M. Pharmacological investigation on Herpestismonniera, Ind J Pharmacy 23 (1961) 2-5.

52 Prakash JC and Sirsi M, Comparative study of the effects of brahmi (*Bacopamonniera*) and chlorpromazine on learning in rats, J SciIndust Res., 21 (1962)93-6.

53 Cook NC and Samman, S, Flavonoids- chemistry, metabolism, cardioprotective effects, and dietary sources, Nutritional Biochemistry, 7 (1996) 66- 76.

54 Bafna PA and Balaraman R, Antioxidant activity of DHC-1, an herbal formulation, in experimentally-induced cardiac and renal damage, Phytother Res., 19(3)(2005) 216-21.

55 Singh S, Eapen S and D'Souza SF, Cadmium accumulation and its influence on lipid peroxidation and antioxidative system in an aquatic plant, *Bacopamonnieri L.* Chemosphere, 62 (2006) 233-46.

56 Govindarajan R, Vijayakumar M and Pushpangadan P, Antioxidant approach to disease management and the role of 'Rasayana' herbs, Ayur J Ethnopharmacol, 99(2005)165-78.

57 Sumathy TS, Govindasamy S, Balakrishna K and Veluchamy G, Protective role of *Bacopamonnieri* on morphine-induced brain mitochondrial enzyme activity in rats, Fitoterapia, (73) (2002) 381-5.

58 Roodenrys S, Booth D, Bulzoni S, Phipps A, Micallef C and Smoker J, Chronic effects of Brahmi (*Bacopamonnieri*) on human memory, Neuropsychopharmacology (27) (2002) 279-81

59 Bhaskar M and Jagtap A, Exploring the possible mechanisms of action behind the antinociceptive activity of *Bacopamonniera*, Int J Ayurveda Res., 2(1) (2011) 2–7.

60 Russo A and Izzo AA, Borrelli, F. Free radical scavenging capacity and protective effect of *bacopamonniera L.* On DNA damage, Phytother. Res, (17) (2003) 870–875.

61 Uabundit N, Wattanathorn J, Mucimapura S and Ingkaninan K, Cognitive enhancement and neuroprotective effects of *Bacopamonnieri* in Alzheimer's disease model, J. Ethnopharmacol, 127(2010) 26–3110.

62 Sudharani D, Krishna KL, Deval K and Safia AK, Priya Pharmacological profiles of *Bacopamonnieri*: a review, *International Journal of Pharmaceutics,* 1(1)(2011)15–23.

63 Kumar N, Thawani V, Gharpure KJ, Naidu MUR and Ramana GV, Efficacy of Standardized Extract of *Bacopamonnieri* on Cognitive Functions of Medical Students: A Six-Week, Randomized Placebo-Controlled Trial, Evid Based Complement Alternat Med, Published online 2016 Oct 10. doi: 10.1155/2016/4103423

64 Janani P, Sivakumari K, Geetha A, Yuvaraj S and Parthasarathy C, Bacoside a down regulates matrix metalloproteinases 2 and 9 in DEN-induced hepatocellular carcinoma, Cell Biochem Funct., 28(2) (2010) 164–9.

65 Das A, Shanker G, Nath C, Pal R, Singh S and Singh HK, A comparative study in rodents of standardized extracts of *Bacopamonniera* and *Ginkgo biloba*: anticholinesterase and cognitive enhancing activities, Pharmacol Biochem Be., 73(4) (2002) 893–900.

66 Achaliya GS, Wododkar SG and Dorle AK, Evaluation of CNS activity of Brahmighrita. Ind. J. Pharmacol, 37 (2005) 33-36.

67 Hasan, Y, Bègue L & Bushman BJ, Viewing the world through "blood-red tinted glasses": The hostile expectation bias mediates the link between violent video game exposure and aggression. Journal of Experimental Social Psychology, 48 (2012) 953–956.

68 Dhanasekaran M, Tharakan B, Holcomb LA, Hitt AR, Young KA and Manyam BV, Neuroprotective mechanisms of ayurvedic antidementia botanical *Bacopamonnieri*, Phytother Res; (21) (2007) 965-9

69 Limpeanchob N, Jaipan S, Rattanakaruna S, Phrompittayarat W and Ingkaninan K, Neuroprotective effect of *Bacopamonnieri* onbetaamyloid-induced cell death in primary cortical culture, J Ethnopharmacol, (120) (2008) 112-7.

70 Mishra M. Memory plus works claim clinical studies, The times of India, 29(1998).

71 Kaur BR, Adhiraj, J, Pandit, PR, Ajita R, Vijay M, Shanta D, Hemangeeni D, Sudha M and Kamble G, Effect of an ayurvedic formulation on attention, concentration and memory in normal school going children, Indian Drugs: 35(4) (1998) 200-203.

72 Jamil SS, Nizami Q and Salam M, *Centellaasiatica* (Linn), Urban o Review, Natural Product Radiance, 6(12) (2007).

73 Singh RH, Narsimhamurthy K and Singh G, Neuronutrient impact of Ayurvedic Rasayana therapy in brain aging," Biogerontology, 9(6) (2008) 369–374.

74 Shukla A, Racik AM, Jain GK, Shankar R, Kulshrestha DK and Dhawan BN, In vitro and in vivo Wound healing activity of asiaticoside isolated from *Centellaasiatica*, J Ethnopharmacol (65) (1999)1-11.

75 Somboonwong J, Kankaisre M, Tantisira B and Tantisira MH, Wound healing activities of different extracts of *Centellaasiatica* in incision and burn wound models: an experimental animal study. BMC Complementary and Alternative Medicine, 12 (2012).

76 Seevaratnam V, Banumathi P, Premalatha MR, Sundaram SP and Arumugam T, Functional properties of *Centellaasiatica* (L.): A review, Int. J. Pharm. Pharm. Sci., 4(5) (2012) 8-14

77 Hashim P, *Centellaasiatica* in food and beverage applications and its potential antioxidant and neuroprotective effect. International Food Research Journal, 18 (7) (2011).

78 Joshi K & Chaturvedi P, Therapeutic efficiency of *Centellaasiatica* (1.) urb. An underutilized green leafy vegetable: An overview, International Journal of Pharma and Bio Sciences, 4(2013)135—149.

79 Inamdar PK, Yeole RD, Ghogare AB and De souza NJ, Determination of biologically active constituents in *Centella Asiatica*, Journal of Chromatography, 742 (1996) 127-130.

80 Singh S, Gautam A, Sharma Aand Batra A, *Centellaasiatica* (L.): A plant with immense medicinal potential but threatened, International journal of pharmaceutical sciences review and research, 4(2) (2010) 9-17

81 Chauhan PK, Pandey IP and Dhatwalia VK, Evaluation of the Anti diabetic effect of ethanolic and methanolic extracts of *Centellaasiatica* leaves extract on Alloxan diabetic rats. Advances in biological research, 4(4) (2010).

82 Chen Y, Han T, Qin L., Rui Y and Zheng H, Effect of total triterpenes from *Centellaasiatica* on the depression behavior and concentration of amino acid in forced swimming mice, Zhong Yao Cai ., 26 (2003) 870-873.

83 Das AJ, Review on nutritional, medicinal and pharmacological properties of Ceu- tellaasiatica (Indian pennywort), Journal of Biologically Active Products from Nature, 4 (2011) 216-228.

84 Lee MK, Kim SR, Sung SH, LIM D, KIM H, Choi H, Park HK, Je,S and Ki YC, Asiatic acid derivatives protect cultured caortical neurons from glutamate inducedexcitotoxicity, Res, Coommon. Mol. Pathol. Pharmocol., 108(1-2) (2000) 75-86.82.

85 Subathra M, Shila S, Devi SM and Panneerselvam C, Emerging role of *Centellaasiatica* in improving age-related neurological antioxidant status, Exp Gerontol, (40) (2005) 707-15.

86 Ponnusamy K, Mohan M and Nagaraja HS, Protective antioxidant effect of cetellaasiatica bioflavonoids on lead acetaticneurotoxicitt, Medical Journal of Malaysia, (63) (2008) 102.

87 Kumar VMH and Gupta YK, Effect of different extracts of *Centellaasiatica* on cognition and markers of oxidative stress in rats, J Ethnopharmacol, (79) (2002) 253-60.

88 Soumyanath A, Zhong Y P, Gold S A, Yu X, Koop D R and Bourdette D, *Centellaasiatica* accelerates nerve regeneration upon oral administration and contains multiple active fractions increasing neurite elongation in vitro. Journal of Pharmacy and Pharmacology, 57(9) (2005) 1221-1229.

89 Wijeweera P, Arnason JT, Koszycki D, and Merali Z, Evaluation of anxiolytic properties of Gotukola--(*Centella asiatica*) extracts and asiaticoside in rat behavioral models. Phytomedicine: International Journal of Phytotherapy and Phytopharmacology, (13) (2006) 668–676.

90 Chivapat S, Chavalittumrong and P & Tantisira MH, Acute and sub-chronic toxicity studies of a standardized extract of *Centellaasiatica* ECa 233, The Thai Journal of Pharmaceutical Sciences, 35 (2011) 55—64.

91 ChivapatS, Chavalittumrong P, Attawish A, Lioonruad T, Bansiddhi J and Phadungpat, S, Toxicity study of *Centellaasiatica* (L) urban. Journal of Thai Traditional & Alternative Medicine, 2 (2004) 3-17.

92 Vohora D, Pal S N and Pillai K K, Protection from phenytoininduced cognitive deficit by *Bacopamonnieri*, a reputed Indian nootropic plant, J ethnopharmacology,71(3) (2000) 383-390.

93 Al-Snafi A E, The pharmacology of *Bacopamonnieri,* A review. International J Pharma Sci Res, 4(12) (2013) 75-92.

94 Sharma R, Chaturvedi C and Tewari P V, Efficacy of *bacopamonnieri* in revitalizing intellectual functions in children, *Journal of Research and Education in Indian Medicine***,** 1 (1987)1–12.

95 Stough C, Downey LA, Lloyd J, Silber B, Redman S, Hutchison C, Wesnes K and Nathan PJ, Examining the nootropic effects of a special extract of *Bacopamonniera* on human cognitive functioning: 90 day double-blind placebo-controlled randomized trial. Phytother Res., 22(12) (2008) 1629-34.

96 Raghav S, Singh H, Dalal PK, Srivastava JS and Asthana OP, Randomized controlled trial of standardized *Bacopamonniera* extract in age-associated memory impairment, Indian J Psychiatry, 48(4) (2006)238-42.

97 Anonymous, Physicians′ Desk Reference for Herbal Medicines, First edition, (Thomson PDR publication), 1999, 1-900. ISBN-10: 1563632926

98 Brinkhaus B, Lindner M, Schuppan D and Hahn EG, Chemical, pharmacological and clinical profile of the East Asian medical plant *Centellaasiatica*, Phytomedicine, 7 (2000) 427-448.

99 Kashmira J, Gohil, Jagruti A. Patel, and Anuradha K. Gajjar, Pharmacological Review on *Centellaasiatica*: A Potential Herbal Cure-all, Indian J Pharm Sci, 72(5) (2010) 546–556.

100 Hughes L, & Cooper C, Understanding and Supporting Children with ADHD: strategies for teachers, parents and other professionals, London: Paul Chapman Publishing, (2007).

101 Purdie N, Hattie J & Carroll A, A review of the research on interventions for Attention Deficit Hyperactivity Disorder: what works best?', Review of Educational Research, 72 (1) (2002)61-99.

102 Lloyd G, Cohen D & Stead J, Critical New Perspectives on ADHD, London: Routledge, (2006).

103 Jensen P, Bhtara V, Vitello B, Hoagwood K, Feil M & Burke L, 'Psychoactive medication prescribing practices for US children: gaps between research and clinical practice', Journal of the American Academy of Child and Adolescent Psychiatry, 38 (5) (1999) 557-565.

104 Ervin R, Kern L, DuPaul G, & Friman P, Classroom-based functional and adjunctive assessments: proactive approaches

to intervention selection for adolescents with attention deficit hyperactivity disorder', Journal of Applied Behaviour Analysis, 31 (1) (1998)65-78.

105 Ervin R, Kern L, Clarke S, & DuPaul G, Evaluating assessment based intervention strategies for students with ADHD and comorbid disorders in natural classroom context', Behavioural Disorders, 25 (4) (2000) 344-358.

106 Srivastava R & Shinde S, ADHD: An emerging market in India', Express Pharma Pulse (2004).

107 Wilcox C, Washburn R & Patel V, Seeking help for attention deficit hyperactivity disorder in developing countries: A study of parental explanatory models in Goa, India, Social Science and Medicine, (64)(2007) 1600- 1610.

108 Malhi P, Singhi P & Sidhu S, Impact of parents and teachers concordance of diagnosing Attention deficit hyperactivity disorder and its sub types', Indian Journal of Pediatrics, 75 (3) (2008) 223-228.