

**Review Article**

**Nootropic plants in Iranian traditional medicine; an overview**

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**ABSTRACT**

Ethnopharmacological relevance: Medicinal herbs have been adopted in Iranian Traditional Medicine (Henceforth ITM) for treatment of neurological diseases for millenniums.

**Aim of the study:** Brain disorders have the highest burden of all diseases in the world with the excessive cost and low impact treatments. The purpose of this review is to augment our knowledge and understanding of traditional approaches to the brain disorders and to unravel new auspicious drugs.

**Materials and Methods:** Major references of ITM were searched for traditional explanations of mechanisms of the brain disorders and its enhancers. After winnowing out the most frequently occurring herbs, their effects on brain disorders in recent studies were probed.

**Results:** The findings revealed 27 medicinal plants that have special effects on the strengthening of the brain tissue and its function.

**Conclusion:** This review demonstrates the protective and restorative effects upon nervous system; effects which have also been verified in the literature of contemporary medicine.

**Key words:** Brain Weakness, Nootropics, Iranian Traditional Medicine

**INTRODUCTION**

The brain is prone to a large spectrum of mental and neurological disorders that approximately is 35% of the burden of all diseases in the world (Olsen, Leonardi, 2003). The total cost of disorders was estimated at 798 billion Euros annually, which is twice as much as that of cancer (Olsen, Leonardi, 2003). These disorders are chronic and highly prevalent that may continue for years. In addition, there is little knowledge about the basic mechanisms of the brain and lack of propitious medications have made the brain disorders become more challenging and complicated than ever (Olsen, Leonardi, 2003)

According to the World Health Organization, complementary/alternative medicine has been expanded globally. Traditional medicine constitutes 65-80% of the world's health care services (WHO strategy, 2002). Iranian traditional medicine (ITM) history dates back to thousands of years ago and it is deemed to have been developed during the medieval times (Ameri et al, 2014). Ancient Persian medical treatises such as Avicenna's Canon of Medicine in 1025 A.D and Razes' Al havi were penned in 960 A.D and both were widely taught in medical centers until the 17<sup>th</sup> century (Siraisi, 1987. Osler, 1921).

Reviews of the ancient medical manuscripts proffer invaluable insights into the turf of natural medications that can boost current medical approaches. In IITM, the organs of the body consist of an amalgam of quadruple humors named akhlat, safra (with warm and dry qualities), sawda (with cold and dry qualities), balgham (with cold and wet qualities) and dam (with warm and wet qualities), these are the mixture of four basic elements viz. water, air, fire and soil. The maladies appear to be spawned by imbalances in the quality or quantity of the humors as substances of the body or in the qualities like warmth, coldness, dryness and wetness (Emtiazi et al, 2013).

Iranian Traditional Medicine has explained neurological diseases in detail (Nikaein et al, 2012). According to the scholars of the ITM, the underlying basic mechanism of all brain disorders is a syndrome called “weakness of the brain (za’fe demagh)”, which makes this organ susceptible to many diseases (Shaharzni, 2008). The treatment approaches fall into two main categories. The first is rectifying the lifestyle which includes mental, physical activities, diet, avoiding sleep disturbances, stressful conditions and living in an enriched environmental housing. The second is applying medications for the disposal of waste materials from the brain and using specific neurotonic agents (Avicenna, 2005).

The present article is a review of the perspectives toward the aforementioned traditional medical approaches for the weakness of the brain. It provides insights into new medications. Moreover, it represents a handful of neurotonic herbs which are used for the prevention and treatment of the weakness of the brain.

## MATERIALS AND METHODS

This study is a literature review elicited from the most pivotal manuscripts of ITM from 9<sup>th</sup> to 18<sup>th</sup> C.E. These manuscripts include *Al-havi* (The Liber Continens, written by Razes in the tenth century CE)(Razes 2001), *Al-Qanoon fi al-Tibb* (The Canon of Medicine, authored by

Avicenna in 1025 CE)(Avicenna1998), *Zakhireh kharazmshahi* (Treasures of the Kharazm shah, created by Seyed Isamail Jorjani in eleventh century CE)(Jorjani 1976) which are in the domain of management of diseases and *al-Shamel fi al-Sana’at e al-Tibbi’ie* (penned by Ibn e Nafis in 1280 CE)(Ibn e Nafis 2007), *Tohfah ol Moemenin* (composed by Mohammad Tonekaboni in 1670 CE)(Tonekaboni 2007). These sources are provided in Noor Software in a modern edition format in languages like Arabic, Persian and English and the search through them was carried out by the keyword Demagh (a persian formal word equivalent to the term “brain” in English).

These books are currently considered the most reliable references in ITM and Pharmacy as well. The resources were explored based upon the following criteria: brain enhancement, clearing the brain, opening up its congestion, improving memory, relieving brain volume loss, dispelling Sawda and Balgham from the brain, preventing the entrance of harmful substances coming from other organs and lack of side effects attributed to the herbal remedies.

Next, modern technical equivalents of the traditional terms were garnered from valid sources such as Flora of Iran in Natural Colors (Ghahreman 1978) and Popular Medicinal Plants of Iran (Amin 2005). The scientific terms were validated taxonomically at [www.theplanetlist.org](http://www.theplanetlist.org). Finally, today’s neurologic effects of the herbal medicine were reviewed through websites such as [pubmed.com](http://pubmed.com), [scopus.com](http://scopus.com) and [scholar.google.com](http://scholar.google.com)

## RESULTS AND DISCUSSION

In ITM, the brain is regarded as the major organ of the whole body and the source of sensory and motor functions. “Zaa’f” or weakness, as the opposite of the word “ghovat” or strength, is a condition in which the decline of the brain’s abilities is observed (Shaharzni, 2008)

Brain weakness is the principal reason of the brain’s inefficiency to eliminate waste materials. The cause of this fragility could be in the brain mass reduction, its porosity, existence of diseases

in other organs of the body such as stomach, liver, uterus and kidney or disturbance in the brain blood circulation(10-14). There are predisposing and precipitating factors such as bleeding, diarrhea, excessive sweating, immoderate physical exercise, sleeplessness, excessive sexual activity, pains and chronic illnesses that trigger pathological changes in the brain (Lucassen et al, 2010).

The clinical manifestations of this syndrome are weakness of mental and neurological functions, opacity of senses, headaches initiated by minimum causes, fear of blood, slowness and difficulty in executive functions, decrease in sexual desire, strong tendency to sleep, pulse weakness and nasal and retropharyngeal discharges (Avicenna, 2005. Jorjani, 1976. Razes, 2002. Ibn al-Nafis, 2008. Cheshti, 2008).

There are two general approaches towards the treatment of weakness of the brain: intervention in the six major health factors and the use of medications. The goal of this treatment is to modify physical properties such as warmth, coldness, wetness and dryness that play pivotal roles in brain diseases and to improve the blood and oxygen delivering and replacement of lost materials from the brain (Ibn al-Nafis, 2008).

#### 1. Intervention in six major health factors

Six quintessential factors ascertain the health condition of the human body which are: weather and climate; food and drink; sleeping and waking; emotional states; absorption and desorption of materials from the body; movement and stillness. By intervention in these six vital health factors, we can impede illnesses. Some examples of these interventions are calorie restriction, dodging insomnia, having physical and mental activity, paying attention to excretion of body materials and avoiding exposure to mental and physical stress. Recent surveys have illustrated that nutrition, exercise and sleep disruption might affect the adult hippocampus volume and neurogenesis (Lucassen et al, 2010). Also, calorie restriction can increase the life expectancy and

reduce development of mental diseases (Weindruch, 1986).

#### 2. Medications

Medicinal interventions based on the opinion of the ITM scholars ameliorate neurological diseases through different mechanisms such as clearing the brain from the waste materials, empowering the brain by consolidating and fragrant herbs, heating up the brain to modify its cold quality, enhancing blood circulation to the brain and improving gastrointestinal functions that ward off associated brain disorders, to name but a few (Ibn al-Nafis, 2008. Cheshti, 2008).

From ITM perspective, there are four stages for digestion. The first takes place in the stomach, the second in the liver, the third in the vessels and the last one in the tissue. In impairment of the organ, the digestive tissue becomes disordered and the materials caused by digestion are amassed or pushed to other organs and consequently, cause disease. Furthermore, the pores in the tissue raise the odds of amassment of the waste materials and increase the susceptibility of the tissue against stress. Therefore, the use of such medicines, which contain hotness or dryness qualities and are consolidating and bring the components of the tissue closer, can boost the organ. Another enhancing mechanism of the organs is the fragrant quality of the herbs. Moderately warming the tissues which are bereft of the sufficient energy for metabolism can accelerate the digestion process. Improving the function of the first and second digestions in the digestive system arms the brain with better chyme and enhances its function (Avicenna, 2005. Ibn al-Nafis, 2008).

In recent years, research on medicinal plants has been performed from neurotropic perspectives. Changing neuro-chemical supplies, oxygenation of the brain and stimulating neural growth, nootropics can reinforce the brain (Dwivedi, 2012). In this literature review, twenty-seven medicinal plants which are widely used in treatment of brain weakness were recognized.

In Table 1 the traditional nomenclatures of the medical plants, scientific names, their quality from the perspective of hotness and coldness or dryness

and wetness, the prescription method and the dosage of the herb in the past and today's neurologic usages in brain disorders are shown.

Traditional name	Scientific name	Quality	Route of administration	Dosage in traditional uses in boiled (gr/daily)	Traditional uses in brain diseases	Current neurobiologic effect
Aftimun (æftim□n) (Tonkaboni, 2007)	<i>Cuscuta epithymum</i> L. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Dry (Tonkaboni, 2007)	Boiled Macerated (Tonkaboni, 2007)	7.5-25 (Tonkaboni, 2007:126)	Removing excessive Sowda of brain, beneficial for depression and epilepsy (Avicenna, 2005. Ibn al-Nafis,2008. Jorjani,1976)	Anti-Convulsive (Mehrabani et al, 2006)
Ostokhodus (□st□x□d□s) (Tonkaboni, 2007)	<i>Nepeta menthoides</i> Boiss & Buhse (Amin,1991. Ghahreman, 1987. Theplantlist.org)	Warm Dry (Tonkaboni, 2007)	Boiled Macerated Powdered (Tonkaboni, 2007)	5-15 (Tonkaboni, 2007:105)	Refining the brain, improves thinking, compatible with old, application in depression, epilepsy, tremor & head traumas, fragrant ( Ibn al-Nafis,2008. Razes,2002).	Neuro-protective, Anti apoptotic (Delshad et al, 2011). Memory enhancer (Ahmadian et al, 2014)
Darcin (da: rtʃi n) (Tonkaboni, 2007)	<i>Cinnamomum zeylancum</i> Blume. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Dry (Tonkaboni, 2007)	Boiled Oil Macerated (Tonkaboni, 2007)	5-15 (Tonkaboni, 2007:385)	Refining the brain and reinforcement of mental power, pain relief, fragrant (Avicenna, 2005. Ibn al-Nafis,2008).	Useful in Alzheimer's disease (Frydman et al., 2011)
So'd (s□□d) (Tonkaboni, 2007)	<i>Cyperus rotundus</i> L. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Dry (Tonkaboni, 2007)	Boiled Macerated (Tonkaboni, 2007)	9 (Tonkaboni, 2007:487)	memory enhancer, mental improvement, fragrant (Avicenna, 2005. Ibn al-Nafis,2008. Jorjani,1976).	Memory enhancer (Rabiei et al., 2013)
Zanjebil (zænd□eb l) (Tonkaboni, 2007)	<i>Zingiber officinale</i> Rose (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Dry (Tonkaboni, 2007)	Powder extract macerated (Tonkaboni, 2007)	5 (Tonkaboni, 2007:461)	anti-amnesic, mental improvement, beneficial in epilepsy and lethargy, stroke and paresis, fragrant (Avicenna, 2005. Ibn al-Nafis,2008)	Memory enhancer (Zeng et al.,2013), Anti-oxidant in Alzheimer disease (Mathew et al., 2014)
Nilofar (n□l fær) (Tonkaboni, 2007)	<i>Nymphaea alba</i> N. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Cold Wet (Tonkaboni, 2007)	Boiled Fermentation Oil (Tonkaboni, 2007)	7-17 (Tonkaboni, 2007:830)	Modification of warmness & dryness in the brain, useful in obsession, sleeplessness and depression (Avicenna, 2005. Ibn al-Nafis,2008)	Anxiolytic (Thippeswamy et al., 2011)
Vard (værd) (Tonkaboni, 2007)	<i>Rosa damascena</i> Herrm(Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Cold Dry (Tonkaboni, 2007)	Boiled Oil Distilled Smell (Tonkaboni, 2007)	28-35 (Tonkaboni, 2007:837)	Reinforcing the brain, fragrant, useful in headache (Avicenna, 2005. Ibn al-Nafis,2008)	Memory enhancer ,learning improvement in Alzheimer's disease(Mohamma dpour et al., 2014.Esfandiary et al, 2014)

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Agir-e-Torki (æg r-e-t r k) (Tonkaboni, 2007)	<i>Acorus calamus</i> L. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Dry (Tonkaboni, 2007)	Boiled (Tonkaboni, 2007)	4.5 (Tonkaboni, 2007:835)	anti-amnesic, removing waste products, mental improvement (Avicenna, 2005. Ibn al-Nafis,2008)	Rejuvenator for the brain (Sharma et al., 2014)cerebrovascular protective (Zhiqiang et al., 2012)
Sib (s b) (Tonkaboni, 2007)	<i>Malus domestica</i> Borkh. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Wet (Tonkaboni, 2007)	Boiled Extract Essence (Tonkaboni, 2007)		Fragrant and reinforcing the brain by strengthening cardia of stomach, useful in obsessions caused by Sawda (Avicenna, 2005. Ibn al-Nafis,2008)	Memory enhancer (Szwajgier et al., 2012) Anti-apoptotic (Chan et al. 2004.2006. Ortiz et al., 2004)
Safarjal (sæfærd æl) (Tonkaboni, 2007)	<i>Cydonia oblonga</i> Miller. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Moderate Wet (Tonkaboni, 2007)	Extract (Tonkaboni, 2007)		Useful in headaches related to GI diseases, vertigo & dizziness (Razes, 2002. Ibn al-Nafis,2008)	Anti-oxidant (Minaiyan et al., 2012)
Bazr-e-Geshniz (bæzr-e-ge n z) (Tonkaboni, 2007)	<i>Coriandrum sativum</i> L. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Cold Dry (Tonkaboni, 2007)	Boiled Maceration (Tonkaboni, 2007)	12.5 (Tonkaboni, 2007:709)	Sedative, useful in headaches, vertigo, dizziness, phobias & epilepsy& mania (Avicenna, 2005. Ibn al-Nafis,2008)	Neuro-protective (Enas et al., 2010), Memory enhancer(Cioanca et al., 2013)
Sonbol (s n b l) (Tonkaboni, 2007)	<i>Valeriana officinalis</i> L. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Dry (Tonkaboni, 2007)	Boiled Fermented Distilled (Tonkaboni, 2007)	4.5 (Tonkaboni, 2007:512)	Removing waste products, reinforcement of brain by decreasing its porosity, fragrant, mild heating the brain, beneficial in headaches (Avicenna, 2005. Ibn al-Nafis,2008. Jorjani,1976)	Anxiolytic (Murphy et al.,2010), anti-convulsive (Rezvani et al., 2010)
Sa'tar (sæ tær) (Tonkaboni, 2007)	<i>Zataria multiflora</i> Boiss. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Dry (Tonkaboni, 2007)	Boiled Vapor Macerated Distilled (Tonkaboni, 2007)	12.5 (Tonkaboni, 2007:560)	Reinforcing the brain, fragrant, mental & sensory improvement, induces mental clarity (Razes, 2002. Ibn al-Nafis,2008)	Cognitive improvement (Majlesi et al.,2012 ),anti-oxidant(Sharififar et al., 2012)
Gharanfol (kæræn f l) (Tonkaboni, 2007)	<i>Eugenia caryophyllata</i> Thunb. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Dry (Tonkaboni, 2007)	Boiled Distillated Fermented (Tonkaboni, 2007)	4.5 (Tonkaboni, 2007:654)	Removing waste products of the brain, mild heating, strong brain reinforce, effective in migraine headache, fragrant& sensory enhancer (Razes, 2002. Ibn al-Nafis,2008)	Memory enhancer(Halder et al., 2012), anti-depression (Mehta et al. 2013)
Felfel (felfel) (Tonkaboni, 2007)	<i>Piper nigrum</i> L. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Dry (Tonkaboni, 2007)	Boiled Extract Macerated (Tonkaboni, 2007)	4.5 (Tonkaboni, 2007:637)	Strong remover of waste products, heating the brain & useful in amnesia and lethargy, beneficial in tremor, paresis and paralysis, improving mental clarity (Jorjani, 1976. Ibn al-Nafis,2008)	Memory enhancer (Hritcu et al., 2014)
lowz (l : z) (Tonkaboni, 2007)	<i>Amygdalus communis</i> L. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Arm Wet (Tonkaboni, 2007)	Boiled Extract Oil (Tonkaboni, 2007)		Best nutrient for the brain, emollient (Ibn al-Nafis,2008)	Nutrient, Anti-oxidant (Sfahlan et al., 2009)

Kondor (kondor) (Tonkaboni, 2007)	<i>Boswellia carterii</i> Bird. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Dry (Tonkaboni, 2007)	Resin Macerated Oil (Tonkaboni, 2007)	2 (Tonkaboni, 2007:725)	Enhances mental clarity, improves thinking, anti-amnesic & refines the brain (Avicenna, 2005. Ibn al-Nafis,2008. Razes,2002)	Anti-convulsive (Jalili et al, 2014)
Bad-e- ranjbooye (ba: d-e- rændz bō je) (Tonkaboni, 2007)	<i>Melissa officinalis</i> L. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Moderate (Tonkaboni, 2007)	Boiled Macerated Distilled (Tonkaboni, 2007)	25 (Tonkaboni, 2007:252)	Memory enhancer, reinforcing the brain and sensory organs (Avicenna, 2005. Jorjani, 1976)	Neuro-protective (Bayat et al., 2012)
Bidmeshk (bidmeshk) (Tonkaboni, 2007)	<i>Salix aegyptiaca</i> L. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Cold Wet (Tonkaboni, 2007)	Boiled Distilled Oil (Tonkaboni, 2007)	50 (Tonkaboni, 2007:369)	Beneficial in headaches, fragrant& reinforcement of brain (Avicenna, 2005. Razes, 2002)	Anxiolytic (Razaei et al., )
Fandogh (fandogh) (Tonkaboni, 2007)	<i>Corylus colurna</i> (Amin, 1991. Ghahreman, 1987. Theplantlist.org)L.	Warm Dry (Tonkaboni, 2007)	Fruit Oil (Tonkaboni, 2007)		Effective nutrient for the brain (Avicenna, 2005. Ibn al- Nafis,2008)	Nutrient, anti- oxidant(Riethmuel ler et al., 2014)
Sabr-e-zard (sabr-e-zard) (Tonkaboni, 2007)	<i>Aloe littoralis</i> Baker. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Dry (Tonkaboni, 2007)	Boiled Macerated (Tonkaboni, 2007)	4.5 (Tonkaboni, 2007:557)	Sedative, useful in headaches, migraines, amnesia, depression, mania, removing waste products of the brain, cognitive enhancer (Avicenna, 2005. Ibn al- Nafis,2008. Jorjani,1976)	Anti-inflammatory (Hajhashemiet al., 2012)
Shaljam (Tonkaboni, 2007)	<i>Brassica rapa</i> var. <i>rapa</i> L. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Wet (Tonkaboni, 2007)	Boiled Extract (Tonkaboni, 2007)		Reinforcing mental powers and enhancing thinking clarity (Ibn al-Nafis, 2008)	Anti-oxidant (Samec et al., 2011. Cartea et al.,2012)
Fostogh (fostogh) (Tonkaboni, 2007)	<i>Pistacia vera</i> L. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Wet (Tonkaboni, 2007)	Boiled Macerated (Tonkaboni, 2007)		Fragrant and reinforcing the brain, improves mental clarity (Ibn al-Nafis,2008)	Nutrient, anti- oxidant (Tomaino et al., 2010)
Tin (tin) (Tonkaboni, 2007)	<i>Ficus carica</i> L. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Wet (Tonkaboni, 2007)	Boiled Macerated (Tonkaboni, 2007)		Useful in obsession, mania and depression, epilepsy& beneficial for mental clarity (Razes, 2002. Ibn al-Nafis,2008)	Memory enhancer (Sumanth et al., 2014)
Calpooreh (kalpooreh) (Tonkaboni, 2007)	<i>Teucrium polium</i> L. (Amin, 1991. Ghahreman, 1987. Theplantlist.org)	Warm Dry (Tonkaboni, 2007)	Boiled Distilled (Tonkaboni, 2007)	7.5 (Tonkaboni, 2007:267)	Memory enhancer, removing waste products, enhances mental clarity (Ibn al-Nafis,2008 )	Anti-oxidant (Tepe et al. , 2011)

**Table 1-** Herbal remedies connected to neurological diseases in ITM.

The following section zeros in on the neurological effects of these herbs in recent studies.

***Cuscuta epithymum* L.**(Convolvulaceae)

*Cuscuta epithymum* L. is a rootless, wholly parasitic plant that belongs to the Convolvulaceae family and is wide spread across the world. It is effective in removing excessive Sawda of the brain and is beneficial for depression and epilepsy.

The percolation extract of it was identified as an effective anti-convulsion remedy.

Data indicated that its extract delayed the onset of seizure and pretreatment of animals diminished the mortality rate significantly. Furthermore, the most effective dose was 100 mg/Kg when administered intra-peritoneal (Mehrabani et al,2006).

***Nepeta menthoides* Boiss & Buhse (Lamiaceae)**

*Nepeta menthoides* Boiss & Buhse as a herbaceous aromatic plant is assigned to Lamiaceae family and is endemic to Iran. It is advantageous in refining the brain and improving the thinking process. It is also compatible with seniors. It is applied in epilepsy, depression, tremor, amnesia and head traumas. Ethanol extract of the aerial parts of it revealed neuro-protective antiapoptotic in axotomy- induced apoptosis of spinal motor neuron in neonate rats when administered intraperitoneal (IP) with the dose of 500 mg/Kg (Delshad et al,2011). Attar et al. displayed that the aqueous extract of *Nepeta menthoides* Boiss & Buhse via IP injection with the dose of 100 mg/kg reversed memory impairments as well as tau hyperphosphorilation which were induced by cold water in rats after 14 days. learning and memory assessed by Morris water maze and tau hyperphosphorilation were gauged by Western Blotting (Ahmadian et al, 2014).

***Cinnamomum zeylancum* Blume (Lauraceae)**

*Cinnamomum zeylancum* Nees as a common spice is a desiccated part of the inner bark of a tropical evergreen tree in India. It has been considered a refining agent of the brain which fortifies mental power and is useful in eliminating the obstructions in the brain. The effects of Cinnamon extract have been evaluated. It has been detected that this natural source inhibited the formation of A $\beta$ -Oligomers and prevented its toxicity on neuronal PC12 cells rectified longevity, recovered locomotive defects and abolished tetrameric species of A $\beta$  in the brain of fly model- of Alzheimer's disease. In this study, the extract served as an efficacious inhibitor of oligomerization and fibrillation of A $\beta$  in vitro and fostered cognitive behavior in vivo on AD mice model, as well (Frydman et al, 2011).

***Cyperus rotundus* L. (Cyperaceae)**

*Cyperus rotundus* L. has worldwide spreading and belongs to the Cyperaceae family. Its rhizomes have therapeutical uses such as being a memory enhancer and mental improving agent. Rabiei et

al. investigated the effect of ethanol extract of its root on learning and memory in the rat model of Alzheimer's disease that received bilateral electric lesions of the Nucleus Basalis Minert using a passive avoidance paradigm and Morris water maze. They maintained that the extract with the dose of 100 mg/Kg has some repairing effects on the memory and behavioral disorders. Besides, this extract was identified as a useful remedy via inducing some changes in Acetylcholine levels in the brain. The evidence displayed that the utilization of the extract for 20 days upgraded motor activity when administered intra-peritoneal with the dose of 100 mg/Kg in rats (Rabiei et al, 2013).

***Zingiber officinale* Roscoe (Zingiberaceae)**

*Zingiber officinale* Rose is a rhizomatous plant in the family of Zingiberaceae whose rhizomes have been used as spice and medicinal herb with multifarious pharmacological activities. It has been acknowledged to be an anti-amnesic agent that improves mental functions and has positive effects in epilepsy, lethargy, stroke and paresis. The experiment by Zeng et al. demonstrated that the administration of ginger root extract reversed behavioral dysfunction and warded off AD-like symptoms in the rat model. The results illuminated that the latency to show significant memory deficits was shorter than in the treatment group and the expression of superoxide dismutase and catalase was unregulated and the rats had low levels of nuclear factor-KB INterlukn-1-beta and Malondialdehyde expression (Zeng et al, 2013). The antioxidant activity, cholinesterase inhibitory, anti-amyloidogenic potential and neuro- protective properties of methanol extract of ginger were investigated. The extract contained 18+- 6.6 mg/g Gallic acid equivalents of total phenolic compound and 4.8 +- 0.69 mg/g quercetin equivalents of dry material. Ginger extract expressed high antioxidant activity on IC50 value in DPPH(2,2-Diphenyl-1-picrylhydrazyl) assay, cholinesterase inhibitory activity in Elman's assay, effectively hindered the formation of A $\beta$

oligomers and increased cell survival (Mathew et al, 2014).

***Nymphaea alba* L. (Nymphaeaceae)**

*Nymphaea alba* N. is an aquatic perennial plant with cup-shaped flowers that have medicinal properties. It has been used for modification of inordinate warmth and dryness in the brain and useful in headaches, insomnia, obsession and meningitis. The ethanol extract of its petal part signified anxiolytic activity using the elevated plus test maze. Light and Dark test, open field test, foot shock induced aggression test and Rota red test for aggressive behavior and motor coordination. The results provided the treatment with 100 and 200 mg/Kg orally which had anxiolytic activity and was a scientific evidence for its traditional claim.

***Rosa Damascena* Herrm (Rosaceae)**

*Rosa Damascena* Mill. is a popular ornamental plant in the Rosaceae family flowers that is commonly used in the production of perfume, food industry and herbal medicine. In ITM, it has been considered as a fragrant herb which fosters the brain and is useful in relieving headaches. The effects of hydro-alcoholic extract of scopolamine induced memory impairment have been evaluated in mice model. Data revealed treatment with 50 and 250 mg/Kg of extract signaled shorter traveled distance and time latency compared with scopolamine group and increased the thiol concentration and decreased malondialdehyde in hippocampus and cortical tissues, suggesting improvement in memory performance in antioxidant effects (Mohammadpour et al, 2014). In line with this, in a research by Esfandiary et al. , *Rosa Damascena* Mill extract elevated spatial learning and memory parameters that restores the decline associated with total hippocampus volume, promotes synaptic plasticity and up-regulates the expression of neurotropic factors in a rat model of Alzheimer's disease (Esfandiari et al, 2014).

***Acorus calamus* L. (Acoraceae)**

*Acorus calamus* L. is a perennial wetland plant that spreads worldwide. Its rhizomes and its active

ingredients are u in medicinal herb studies for uprooting waste products and enhancing the brain. In addition, it has been regarded as an anti-amnesic herb that has beneficial effects in epilepsy and aphasic disorders. In the review by Sharma V et al, *Acorus calamus* L. was presented as a rejuvenator for the brain and the nervous system (Sharma et al, 2014). Also, cerebrovascular protective beta-asarone in AD rats has been assessed using Morris water maze for behavioral responses, cerebral blood flow (CBF), determination of lactic acid and pyruvic acid and sodium potassium ATPase activity. The evidence proves its effects on improvement in memory performances. While the CBF was higher , lactic and pyruvic acids were lower and the activity of the sodium potassium pump was higher than that of the control group in AD model rats (Zhiqing et al, 2012).

***Malus domestica* Borkh. (Rosaceae)**

*Malus domestica* Borkh. is a domesticated apple from Rosaceae family that is one of the most cultivated fruit trees in the world. It is a fragrant herb that reinforces the brain and is useful in obsessions caused by excess Sawda in traditional terms. Szwajgidr et al. came to identify anti-cholinesterase activity in the apple juice that gives credence to its possible potentials in the context of restoring the cognitive function and improving the memory in vitro (Szwajgier et al, 2012). Chan et al. contended that the supplementation with apple juice concentration prevented presenilin 1 over expression as a propagator of oxidative stress factor and diminished generation of Beta- amyloid fibrils in Murine rats. (Chan et al, 2004. 2006). Another study by Ortiz D et al. showed that apple juice prevented -induced calcium influx apoptosis as the consequences of free radicals ( Ortiz et al, 2004).

***Cydonia oblonga* Mill (Rosaceae)**

Cultivated for countries, *Cydonia oblonga* Miller. is a seasonal fruit tree from Rosaceae family. In ITM, it has been taken to be a useful fruit in headaches pertinent to GI diseases, vertigo and dizziness. In a study by Minaiyan et al., it was

exhibited that queans juice and its hydro alcoholic extract in doses ranging from 500 to 800 mg/kg resulted in significant alleviation in ulcerative colitis in rats, owing to possessing antioxidant activities (Minaiyan et al,2012).

#### **Coriandrum sativum L. seed (Apiaceae)**

*Coriandrum sativum* L., as an annual herb, belongs to the Apiaceae family that its seed is used widely in seasoning food and traditional medicine for headaches, insomnia, vertigo, dizziness and epilepsy. Protective effects of *Coriandrum sativum* L. seed in form of aqueous extract was applied against neuro- degeneration in  $AlCl_3$ - induced AD male Albino rats. It was unveiled that coriander seed revived pyramid cells to normal and, after stopping  $AlCl_3$  administration of coriander, repaired those cells (Enas et al, 2010). Besides, the effects of inhaled coriander volatile oil (1%-3% daily for 21 days) were evaluated in  $A\beta$  treated rats. The findings signified positive effects on spatial memory. It was also manifested that the oxidative stress markers in the hippocampus were significantly dwindled. In addition, anti-apoptotic activity was determined in the absence of DNA cleavage patterns (Cioanca et al, 2013).

#### **Valeriana officinalis L.(Caprifoliaceae)**

*Valeriana officinalis* L., as a flowering perennial plant belonging to the Caprifoliaceae family, has worldwide spreading and is introduced for its medicinal uses. It has been maintained to be a fragrant herb that gets rid of the waste products of the brain, boost it by shrinking its porosity and has mild heating properties which decrease excessive wetness in the brain. Anxiolytic effects of *Valeriana officinalis* root extracts have been evaluated in rats using an elevated plus maze. A significant reduction in anxious behavior was noted when either valeriana root extract (3 mg/Kg) or valerenic acid (3 mg/Kg) eas was administered (Murphy et al, 2010). Furthermore, aqueous extract of Valerian (200-500 mg/Kg IP) and petroleum ether extracts (50-100 mg/Kg Ip) were administered in an experimental model of temporal lobe epilepsy in rats. Notable anti-

convulsive effect of the herbal extract through activation of adenosine system was observed (Rezvani et al, 2010).

#### **Zataria multiflora Boiss.(Lamiaceae)**

*Zataria multiflora* Boiss. as a valuable medicinal and condimental herb belongs to the Lamiaceae family and is used in folk medicine for its different properties such as reinforcing the brain, mental and sensory improvement, induction of mental clarity and having positive effects in tinnitus. The effect of *Zataria multiflora* Boiss. essential oil on mental abilities in  $A\beta$ - induced cognitive deficits in a rat model of AD has been evaluated. The findings illustrated that the essential oil restored impairment in cognitive functions (Majlesi et al, 2012). In another study the essential oil and methanol extract of this herb have been studied using Elman and DPPH methods. Data revealed that the essential oil and methanol extract anti-cholinesterase activity were  $95.3 \pm 3.4 \%$  and  $87.9 \pm 2.2 \%$  and the inhibitory effect of DPPH free radical were  $98 \pm 2.4\%$  and  $93.2 \pm 1.7 \%$  (Sharififar et al, 2012).

#### **Eugenia caryophyllata Thunb.(Myrtaceae)≈ Syzygium aromaticum (L.) Merr and L.M. Perry**

*Eugenia caryophyllata* Thunb. is a scientific name of flower buds of an evergreen perennial tree that belongs to the Myrtaceae family. It is used as spice and in formulation of pharmaceutical and therapeutical products. It has been adopted for eradicating waste products of the brain and reinforcing the brain and sensory organs as a fragrant herb and is effective in depression, migraine headaches and post nasal discharges. The cognitive effect of clove oil on memory deficits have been examined in scopolamine-induced memory disordered rats by using elevated plus maze. Clove oil with the dose(0.1 mg/Kg IP) proved to be significantly restorative in acquisition and retention deficits (Halder et al, 2012). Furthermore, it was administered via IP (intra-peritoneal) to evaluate depression by using Forced swim test(FST) and total suspension test(TST). The loco motor activity by photoactometer procedure and Rota rod test were assessed.

The findings demonstrated significant decline in duration of immobility in FST and TST, increase in loco motor activity in photoactometer procedure and enhancement in muscle coordination in Rota rod test. It also lowered depression with the dose of 0.05 and 0.1 ml/kg (Mehta et al, 2013).

**Piper nigrum L. (Piperaceae)**

*Piper nigrum* L. is known as the king of spices and belongs to Piperaceae family. It is dried pungent, fruit, boiled, extracted, macerated and its oil was used in seasoning and herbal medicine. It is assumed to be a strong remover of waste products and a heating agent of the brain. It is also of help in amnesia, lethargy, tremor, paresis and paralysis in ITM. The memory enhancing possessing antioxidant features of *Piper nigrum* L. has been evaluated by A $\beta$  rat model. It was found that the administration of the extract decreased glutathione, Malonaldehyde and protein carbonyl levels, serving as oxidative stress markers. It has also been displayed that it fostered memory performances in maze tasks (Hritcu et al, 2014).

**Amygdalus communis L. (Rosaceae)  $\approx$  Prunus dulcis (Mill) D.A. Webb**

*Amygdalus communis* L. is a deciduous tree in the Rosaceae family. It is supposed to be a rich source of nutrients and has health-promoting components. In traditional herbal medicine, it is known as the best nutrient for the brain. Esfahlan et al. pinpointed antioxidant capacity of various parts of *Amygdalus communis* L. among different genotypes. Data revealed S3-7 with the highest phenolic component, represented significant scavenging activity for hydrogen peroxide, nitrite and superoxide (Sfahlan et al, 2009).

**Boswellia carterii Bird. (Burseraceae)  $\approx$  Boswellia sacra Fluek.**

*Boswellia carterii* Bird. is a branching tree found in Asia. Its oleoresin has been used in traditional medicine to refine the brain, enhance mental clarity and boost memory and thinking. The aqueous extract of *Boswellia* was administered via IP (intra-peritoneal) in temporal epileptic rat

model as a consequence of kindling by pentylenetetrazole. The findings exhibited that the extract significantly declined the number of neuronal processes in CA1 region, improved learning deficits and eliminated adverse cognitive effects of seizure with the dose of 1 g/day (Jalili et al, 2014).

**Melissa officinalis L. (Lamiaceae)**

*Melissa officinalis* L. is a perennial herb in the mint family Lamiaceae, native to western Asia. This herb has been used in folk medicine for a sundry of medical purposes, particularly in nervous complaints, memory enhancement, brain reinforcement and sensory organs. The protective effects of *Melissa officinalis* after ischemic brain injury have been explored in vitro and in vivo in rats. Protection in hypoxia in cultured neurons with the dose of 10 mg/kg was observed. Treatment with the herb efficaciously reduced caspase 3 activity and pro inflammatory cytokines levels as the consequences of ischemia (Bayat et al, 2012).

**Salix aegyptiaca L. (Salicaceae)**

*Salix aegyptiaca* L. is a flowering deciduous tree belonging to Salicaceae family and is cultivated in Mediterranean region. Its extracts and essential oils have different pharmacological activities against insomnia, anxiety and headache as a fragrant herb through reinforcement of the brain. The anxiolytic characteristics of *Salix aegyptiaca* extract were probed in rats using elevated water maze before anesthesia which represented significant improvement in behavioral responses and increased the proclivity to sleep with the dose of 200 mg/kg in comparison to diazepam (Razaei et al, ).

**Corylus colurna L. (Betulaceae)**

*Corylus colurna* L. is a deciduous tree which spreads from Balkan to northern of Iran and belongs to Betulaceae family. Its seed has been supposed to be a source of nutrients with pharmacologically valuable and natural elements. In traditional herbal medicine it has been surmised to be an effective nutrient for the brain. In a research by Reithmuller et al., the anti-oxidant

phenolic compounds of *Corylus colurna* were presented. It was acknowledged that those components possessed potent scavenger activities in both DPPH(2,2-Diphenyl-1-picrylhydrazyl) and ABTS(2,2'-Azino-bis(3-ethylbenzothiazoline-6-sulphonic acid) free radicals and high polyphenolic content that showed significant correlation with antioxidant activity (Riethmueller et al, 2014).

**Aloe littoralis Baker. (Xanthorrhoeaceae)**

*Aloe littoralis* Baker. is a succulent herb that belongs to Xanthorrhoeaceae family. It has been used in traditional medicine in the forms of crude resin, boiled or maceration in vinegar to treat headache, amnesia, insomnia and mania by removing waste products of the brain and enhancing cognitive function through gastric cleaning. Novel studies have shed lights on its anti-inflammatory effects. Hajhashemi et al. applied *Aloe littoralis* baker raw mucilaginous gels (12.5 and 100%) topically for 24 days in incision and thermal wound model rats. They managed to demonstrate notable efficacy in healing and controlling inflammation (Hajhashemi et al, 2012). More investigations and empirical evidences are needed in order to glean the neurological effects that are claimed in traditional uses.

**Brassica rapa L.(Brassicaceae)**

*Brassica rapa* Var . *rapa* L. as an annual herb, is one of the oldest worldwide cultivated crops that belongs to Brassicaceae family. Its root and seeds have been used in reinforcing the brain and improving mental clarity. The phenolic compositions of *Brassica* species including phenolic acid, hydrocinnamic acid and flavonoids were determined (Samec et al, 2011). In addition the antioxidant activity of the phenolic content were assessed by DPPH and ABTS radical scavenging assays. Data indicated a potent anti oxidative capacity in the herb (Cartea et al, 2010)..

**Pistacia vera L.(Anacardiaceae)**

*Pistacia vera* L. is one of the popular nuts, native to western Asia and Middle-East which is of

Anacardiaceae family. It is known as a valuable source of nutrients and has been used traditionally in the form of crude, boiled, powder and maceration to improve thinking and mental clarity. It is also used as a fragrant to reinvigorate the brain. The antioxidant activity and phenolic composition of *Pistacia vera* L. by means of DPPH, Folin-ciocalteau colorimetric method, TEAC and SOD-mimetic assays have been evaluated. Significant antioxidant activity in both seeds and skins were proved, but the contents of phenolic compounds were higher in the skins (Tomaino et al, 2010).

**Ficus carica L.(Moraceae)**

*Ficus carica* L. is a deciduous tree in the Moraceae family that originated in the Mediterranean. It is known as a good nutrient and has medicinal uses in traditional practice in epilepsy, obsession, mania and improving mental clarity it has been used in different forms such as crude, aqueous extract, boiled and maceration. In the study by Sumanth et al, the ethanolic fruit extract of *Ficus carica* was tested on rats to assess the learning and memory enhancing characteristics, using elevated water maze, Hebb William maze and Morris water maze. Transfer latency, time taken to reach reward chamber and swim latency significantly dropped after treatment with the dose of 200, 400mg/kg orally (Sumanth et al, 2014).

**Teucrium polium L.(Lamiaceae)**

*Teucrium polium* L. is a wild-growing flowering plant which is found in Asia, Europe and Africa. It belongs to the Lamiaceae family and has been employed in Traditional herbal medicine in the form of powder or boiled for uprooting waste materials from the brain and improving memory and mental clarity. The anti-oxidant and DNA protective properties of *Teucrium polium* water extract were delineated in vitro. Data demonstrated notable protection for native DNA in the dose of 40 mg/ml and high phenolic and flavonoids in the extract (Tepe et al, 2011). Herbs including *Cuscuta epithimum* L., *Nepeta menthoides* Boiss & Buhse, *Cinnamomum zeylancum* Nees, *Cyperus rotundus* L., *Zingiber*

officinale Rose., *Rosa damascena* Mill, *Acorus calamus* L., *Valeriana officinalis* L., *Zataria multiflora* Boiss., *Eugenia caryophyllata* Thunb., *Piper nigrum* L., *Boswellia carterii* Bird., *Brassica rapa* Var. *rapa* L., *Melissa officinalis* L., *Salix aegyptiaca* L., *Aloe littoralis* Baker. And *Teucrium polium* L. are beneficial in reinforcement by purification and removal of waste materials from the brain.

*Rosa damascena* Mill, *Malus domestica* Borkh., *Cydonia oblonga* Miller., *Coriandrum sativum* L., *Valeriana officinalis* L., *Zataria multiflora* Boiss. and *Pistacia vera* L. are useful in preventing various toxins from damaging the brain, decreasing its porosity and strengthening stability in the nervous system.

*Cyperus rotundus* L., *Zingiber officinale* Rose, *Acorus calamus* L., *Piper nigrum* L., *Boswellia carterii* Bird. *Melissa officinalis* L., *Pistacia vera* L. and *Teucrium polium* L. are effective in memory and thinking enhancement by purifying the brain and modifying the abnormal qualities.

The herbs for restraining the brain's volume loss are *Amygdalus communis* L., *Corylus colurna* L. and *Ficus carica* L.

## CONCLUSION

Brain disorders are assumed to be serious challenges amongst all diseases. In ITM, in addition to extrinsic predisposing and precipitating factors, brain tissue's intrinsic susceptibility to illnesses is of paramount importance, too. Therefore, the aim of this paper was to seek for herbal remedies which are mostly effective on brain's internal tendency toward diseases or brain's weakness. Unless treated, brain weakness leads to the accumulation of waste materials, the creation of obstruction, increase in the vulnerability of the brain against stress, impaired memory and cognitive functions and brain tissue volume reduction. Therefore, given the wide clinical spectrum of the brain weakness from ITM perspective, coming to find powerful brain enhancers for a wide range of mental illnesses can be more than useful, especially

regarding to the fact that some nootropic agents have nutritional properties. It should be mentioned that positive neurologic effects of the aforementioned plants have been detected in studies on animals; for wider application and providing more cogent evidence, however, further studies are warranted. The researchers of the present study, taking into account the above hypotheses, aim to scrutinize the effect of nepeta on Alzheimer's disease and are performing clinical trials in this regard. It should be stated that ethologic Alzheimer has been thoroughly enunciated in ITM and one of the most vital causes has been reported to be brain weakness which aggravates with aging.

With regard to the saliency of hotness and dryness qualities from among the nootropic agents, it seems these qualities, in analyzing the medical effects, ought to be given more attention.

As it was noted, revising the lifestyle can also have a special place in treatment of the brain weakness. The evidences and results for this type of treatment are available at the academic communities all over the world. In ITM, the method for modifying the lifestyle for each organ has a particular instruction to improve the brain or stave off the occurrence of the disease that can be presented as Organ Specific Lifestyle. Regarding to the fact that the Neurological diseases are growing apace, especially due to manifold unknown factors, lifestyle modification, specified for nervous system, can go a long way in forestalling these types of diseases.

Based upon several centuries of experiences, there also exist other mechanisms in treatment of brain weakness such as modification of warm, cold, wet and dry qualities and reduction of brain porosity which can provide a new foundation for novel drugs and open a promising horizon for future studies.

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