Cases of Alzheimer's disease are expected to triple by 2050[0]. Neurodegenerative diseases are increasing around the world. [1] The most common degenerative nerve diseases are: [Alzheimer disease, Multiple Sclerosis, Parkinson disease, Lewy Body Dementia, Frontotemporal Dementia, Amyotrophic Lateral Sclerosis(ALS), Huntington Chorea, and Prion Diseases]. Neurofibrillary tangles and many kinds of striatal amyloid plaques are identifiers Alzheimer's and Parkinson's and Dementia. This nerve damage causes loss of motor control and loss of memory.

A mild case of neurodegeneration has been presumed to be normal aging – The term "Senior Moment" is in the dictionary. Cognitive aging may actually be an earlier stage of Parkinson's or another neurodegenerative disease as opposed to a normal aspect of aging like grey hair.[3] Dementia affects 1 in 20 people over the age of 65. The age-specific incidence of dementia in the UK increases from 7/1000 per year at age 65 to 85/1000 per year at age 85.[6] In a US study, about 2.5% of subjects aged 65 to 74 years had a clinical diagnosis of senile dementia compared to 4% of those aged 75 to 79, 11% of those aged 80 to 84 and 24% of those aged 85 to 93.[7] Additionally, many more people suffer from mild cognitive impairment that does not progress to dementia.

In the late 1990's it first became accepted knowledge that humans have the ability to create new neurons. I was previously thought that we were born with all the neurons we will ever have and that we can only lose them, however we now know of the process called neurogenesis.[9][10] It is now known that medicines causing the inhibition of the acetylcholinesterase (AChE) enzyme improve cognitive abilities for neurodegenerative diseases. AChE inhibitors currently serve as front line medication for Parkinsons and Alzheimers. They also have been found to improve behavioral and psychological symptoms of dementia. [2]

To aid in the understanding cholinergic principles, consider Datura Stramonium from the nightshade family which is an anticholinergic agent, a substance that blocks the neurotransmitter acetylcholine. Classified as a deliriant, it causes bizarre behavior and pronounced amnesia. The effects from Datura poisoning generally last from 24-48 hours and in some cases, it can last 2 weeks. [13] The common-knowledge antidote is a reversible cholinesterase inhibitor, Physostigmine, interestingly - acquired from the poisonous Manchineel tree. [14]

There are multiple reversible AChE inhibitors that have varying methods of action based on their classification of competitive, noncompetitive, or a degree of mixed inhibition that determines the duration and bonding affinity between the inhibitor and the acetylcholinesterase enzyme. As of 2018, three acetylcholinesterase (AChE) inhibitors donepezil, galantamine and rivastigmine are recommended as options for managing Alzheimer's disease. Guidance note 1.4 says "If prescribing an AChE inhibitor (donepezil, galantamine or rivastigmine), treatment should normally be started with the drug with the lowest acquisition cost" [12]

Deoxypeganine is an Alkaloid from Syrian Rue (Peganum Harmala), a plant used extensively in traditional medicine in lands with an Islamic heritage for CNS and other ailments. This compound is shown to have acetylcholinesterase inhibitory activity twice that of Galantamine." [15] This knowledge is not being utilized by mainstream medicine. Additionally, it has been proven that harmane, harmine, and harmaline, the main active constituent in Syrian Rue, had good selective inhibitory activities against acetylcholinesterase. [17] 80 extracts were screened for AChE inhibitory activity by a TLC bioautography method. The inhibiting effect of the 32 most active extracts was measured by a microplate colorimetric assay. Due to the best activity, the seeds of Peganum harmala L. were investigated in detail. [11]

In 2017 mankind first discovered 10 additional alkaloids in Peganum harmala. Their alkaloids structures, including stereochemistry, were elucidated through spectroscopic analyses, quantum chemistry calculations, and single-crystal X-ray diffraction. [18] In the Tihkal under the harmaline entry it mentions that the effects of pure harmaline by itself, differ from the effects of *Peganum harmala* whole seeds. Shulgan wrote, "They are very different from one-another." Other researchers concur with Shulgans findings.

It has also been noted by experiential researchers that the inhaled effects from Syrian Rue smoke differ from oral digestion. It is possible that heat decarboxylates part of the medicine as is the case with tetrahydrocannabinol. [19] Interestingly, it has also been shown that the main active ingredient in cannabis, tetrahydrocannabinol (abbreviated THC), is also a competitive inhibitor of acetylcholinesterase.[16] Furthermore, In Islam, according to the Shi'a hadith, Muhammad was commanded by God to have his people ingest Syrian Rue for bravery. This Hadith is interesting in the present connection because it is followed by the recommendation not that it be ingested, but that it be burned as incense instead. In an older text, another hadith indicates that Syrian Rue was consumed orally in a drink made with milk. [20] Because it is known that Syrian Rue contains a minimum of 4 different alkaloids which act as acetylcholinesterase inhibitors, and it is known that there are subtle differences in each inhibitors selectivity and duration, it would reason that the seeds as a whole are a more effective medicine than any alkaloid that is singled out from them. Leonardo da Vinci wrote that Syrian Rue is "miracle smart nutrient" and he was neither Islamic nor aware of neurofibrillary tangles and amyloid plaques. Syrian Rue apparently flosses your neurons and brushes your brain.

Syrian Rue is not the only natural plant medicine. Marijuana[16] is scientifically known to be in the same medicinal category as donepezil, galantamine and rivastigmine which are the leading prescriptions for the leading problem plaguing humanity as we enter 2018. Sacred Plant medicines will be recognized as we exit 2018. Levels of neurotoxic b-amyloid peptides are significantly decreased in postmortem examinations of Alzheimer's victims.[4] Nicotine produces clarity and cognitive improvement when the Nicotinic acetylcholine receptors(nAChRs) are activated.[5] The tobacco plant has greater medicinal activity when used as a snuff for insufflation.

Coffee, tea, and caffeine consumption have been found to have preventive effects on cognitive decline and dementia. Beyond the short-term enhancing effects, some studies examined the long-term effects and showed that coffee, tea, and caffeine consumption could contribute to protect against late-life cognitive decline and dementia.[8] It was discovered that there is a neuronic layer routing electrical neuroblasts in stimulated neurons near neurogenesis.[21] Electrical activity also stimulates the making of small fibers that assist the migration of newborn neurons [22] Exciting the neurotransmitters serotonin, acetylcholine, dopamine, and glutamate have been identified as factors in stimulating neurogenesis.[23] We have known for a while that exercise produces serotonin and dopamine.[24] We know now that introducing those neurotransmitters also promotes neurogenesis. Increased neurogenesis has been observed by both enriched environment stimuli and exercise. [25]

Antidepressant Treatment Increases Hippocampal Neurogenesis [26]. Others have confirmed the induction of neurogenesis by antidepressant drugs.[27] [28] Antidepressants that enhance serotonergic signaling stimulate hippocampal neurogenesis by a mechanism that may involve upregulation of BDNF. These drugs raise serotonin and dopamine levels. Interestingly, the strongest type of Antidepressant is inhibition of monoamine oxidase, an MAOI. Due to the dangers of synthesized pharmaceutical

irreversible MAOI's they are only prescribed as a last resort. Therefore, Syrian Rue is a multi-faceted medicine for promoting neurogenesis because it also functions as a very potent reversible MAOI medicine.

One study finally looks beyond the acetylcholinesterase inhibition aspect to study the whole-medicine cerebroprotective effect of the isolated total alkaloid extract of Peganum harmala by its antioxidant characteristic in ethanol influenced oxidation by increasing the GSH and decreasing the TBARS level in whole brain, which delays the neurodegenerative process. The cerebroprotective effect was further adorned by its MAO-A inhibitory action, by which it influences the effects of epinephrine and other monoamines. It prevented the DNA fragmentation of frontotemporal cortex of the brain by decreasing in the internucleosomal DNA fragmentation and lowering the laddering pattern. Hence, all these preventive measure of harmal alkaloids of seeds of Peganum harmala are potential enough in the management of Neurodegenerative disorders of the type Alzheimer's diseases.[29]

If binding more serotonin at receptor sites promotes neurogenesis it is likely that plant sources of natural analogs of Dimethyltryptamine(DMT), which are psychedelic tryptamines or serotonergic psychedelics, such as 4-AcO-DMT, 5-MeO-DMT, 5-HO-DMT, psilocybin (4-PO-DMT), and psilocin (4-HO-DMT) binding to the same receptor sites as serotonin, may also promote neurogenesis.

Finally, sex hormones (estrogen and testosterone) may directly and/or indirectly affect neurogenesis in the aging brain. For example, estrogen levels decline abruptly in post-menopausal women not receiving hormone replacement therapy. Estrogen deprivation significantly reduces hippocampal BDNF levels in the female rat hippocampus; Estrogen alone promotes proliferation of both embryonic and adult neural stem cells (Brannvall, 2002). Similarly, men experience an age-related decline in testosterone levels. Testosterone promotes neurogenesis in the adult songbird neostriatum (Louissaint *ci a!.*, 2002)

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