β-Carbolines: Neuropharmacology

Beta-Carbolines: Enhancing CNS function, Neurogenesis, Anti-Alzheimer's, Anti-cancer, Antidepressant, restored cellular proliferation

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[Abstract]

Beta Carbolines stimulate the CNS protecting against conditions of neurodegeneration and impacting the cellular proliferation cycle acting as protein kinase inhibitors causing the production of needed cells and inhibition of cancerous and mutant cell propagation which occurs due to dysfunction in the neural system corrected by beta carbolines. Beta Carbolines inhibit DYRK1A, MAO, and AChE. They enhance GABAA receptor responses and astrocytic function, supporting neuronal survival and synaptic plasticity. This study reviews established findings, use in antiquity, then documents observations from use in practice.

Peganum Harmala, called Syrian Rue, contains harmine and other beta carbolines. Seeds from Peganum Harmala provided the whole spectrum of beta carbolines used in this study. Practical dietary requirements are discussed. This investigation concludes to show that serious adverse dietary or drug interaction is uncommon and preventable allowing for regular use of beta carbolines to prevent neurodegeneration, cancer, and osteoporosis. Increased or restored neural function has wide-ranging applications in medicine. As an inhibitor of DYRK1A it promotes human beta cell production and shows potential to accompany stem cell treatments. In vitro studies are only suggestive preclinical evidence of the neuropharmacological effects however the results suggest numerous applications in medicine including treating Type 2 diabetes because of increased beta cell production. The first clinical human studies to determine dose and safety were published in 2025.(NCT05162686 and NCT05526430)

[Introduction]

Beta-carbolines act as potent modulators of brain chemistry and astrocytic activity stimulating neurotrophic signaling which support neuronal survival and synaptic plasticity. They enhance GABAA receptor responses which in turn which can lead to neurogenesis. They promote remyelination, synaptic protein restoration, and nerve health while elevating monoamine neurotransmitter levels. At low doses leading to enhanced CNS function. At high doses beta carbolines are neurotoxic and produce mild to extreme nausea.

Here is laid out all the known traits of this plant in medicine followed by different medicinal fields of study which intersect at the beta carboline.

Antibacterial, antiprotozoal(kills free living and parasitic protozoal organisms), antimutagenic/ antigenotoxic/genoprotective(1. Moura et al., 2007), preventative of DNA damage(2. Senhaji et al.,2022), antimicrobial, antifungal, antiviral, antioxidant, anti-inflammatory, antidepressant, antipiroplasmic(kills piroplasmic parasite), anthelmintic(kills tapeworms), antiseptic, antipyretic(reduces fever), antitumor(3. Dai et al., 2012), anticancer and antidiabetic for Type 2 diabetes(4. Wang et al., 2023). Insulin-signaling dysregulation was ameliorated, and GLP-1 levels elevated after the administration of *Peganum harmala* seed extract for 4 weeks.(5. Saleh et al.,2021) Multiple studies have confirmed these qualities.(6. Sharma et al., 2022; 7. Moloudizargari et al., 2013; 8. Sharifi-Rad et al., 2021) One study found harmine to be more effective than stem cell treatments for pancreatic beta cell production.(9. Rosselot et al, 2024)

The beta-carbolines in *Peganum Harmala* have been proven to be medicinally helpful for:

leukemia(10. Zaker et al., 2007), lower urinary tract symptoms(11. Saeidi et al., 2015), dermatoses(12. El-Rifaie, 1980), bronchitis and asthma(13. Liu et al., 2015), influenza(14. Moradi et al., 2017) and leishmaniasis(15. Rahimi-Moghaddam et al., 2011) which is a wide array of clinical manifestations caused by parasites of the Trypanosomatida genus. Harmine is also a vasodilator/vasorelaxant(16. Shi et al., 2000), aphrodisiac(17. Subhan et al., 1998; 18. Enema et al., 2018) and cognition enhancing(19. Santos & Hallak, 2017; 20. Shu-Ping et al. 2018) as an Acetylcholinesterase inhibitor(AChEi)(21. Adhami et al., 2011) and butyrylcholinesterase inhibitor(BChEi)(22. Zhao et al.,2013) Harmine also induces osteogenesis(bone regrowth) and prevents bone loss by suppressing osteoclastogenesis (23. Yonezawa et al., 2011; 24. Patel et al., 2012; 25. Chen et al., 2020) and promotes neurogenesis(the birth of a neuron in brain growth or repair) (26. de la Fuente Revenga et al., 2015; 27. Morales-García et al., 2017; 28. da Cruz et al., 2023) and is restoring astrocytic functions(29. Li et al., 2011; 30. Liu et al., 2017) upregulating astroglial glutamate transporters removing excess glutamate from the synaptic space protecting neurons and preventing excessive intracellular calcium which accumulates in mitochondria and triggers cellular death.(31. Eunhee Kim et al. 2021; 32. Gielecinska et al.,2024) Reducing glutamate is a thereputic aim in treating epilepsy. Excess glutamate contributes to neurodegenerative disease.(33. Todd & Hardington,2020; 34. Verkhratsky et al.,2023) Harmine is also an inhibitor of cyclin dependent kinases(CDK), protein kinase DYRK1A(35. Göckler et al., 2009; 36. Frost et al., 2011) and others which are key regulators of the cell proliferation cycle(37.Song et al., 2002; 38. Song et al., 2004). CDK inhibitors are also past and future in cancer treatment.(39. Asghar et al., 2015; 40. Ahmad et al., 2020) It is also an MAO inhibitor.(41. Herraiz et al., 2010; 42.

Herraiz & Guillén, 2018) Harmine has been shown to reduce anxiety by inhibition of neuroinflammation.(43. Zheng et al, 2023)

[Cancer]

As confirmed in recent research, the beta carbolines in *Peganum Harmala* show anticancer activity. Numerous types of cancerous cell growth are inhibited, including breast cancer(44. Ding et al., 2019), pancreatic cancer(45. Wu et al., 2019), ovarian cancer(46. Gao et al., 2017), gastric cancer(47. Li et al., 2017) and others. In fact, most beta-carbolines exhibit anticancer effect can augment cancer treatment solutions being used. Beta-carbolines, particularly harmine and harmol, exhibit promising anticancer properties by inducing apoptosis and inhibiting proliferation in various cancer cell lines.

Beta-carbolines induce neuroendocrine response, restore central nervous system cellular function(5. Saleh et al., 2021), and protect against oxidative damage of brain mitochondria and synaptosomes(48. Kim et al., 2001) suggesting protection against neurodegeneration.

[Alzheimer's]

The spectrum of Beta Carbolines in *Peganum Harmala* inhibit acetylcholinesterase, thereby reducing acetylcholine metabolism. Alzheimer's patients are given AChEi's(acetylcholinesterase inhibitors), to raise acetylcholine levels with more potent effect than *Peganum Harmala*.(49. Ibach & Haen, 2004; 50. Galimberti & Scarpini, 2016) Acetylcholine is the substance of focus in memory supplements.(51. Hasselmo, 2006) *Peganum Harmala* is an AChEi which increases the

levels of the neurotransmitter acetylcholine by reducing the metabolism rate of acetylcholine.(52. Yang et al., 2015) Acetylcholine is responsible for its role in memory recall and for its cognitive enhancing effects. It also is used the dream state of the mind. Acetylcholinesterase(AChE) is closely related to Butyryl Cholinesterase(BChE). *Peganum Harmala* is also a proven BChE inhibitor as well.(53. Tundis et al., 2016) Additionally, recent knowledge collectively recognizes that MAO inhibitors have proven as effective therapeutic agents for the treatment of Alzheimer's disease.(54. Manzoor & Hoda, 2020) Furthermore, Beta-carbolines such as harmine, harmol, norharmane, harmaline have a high affinity for DYRK1A and modulate multiple sites on the Tau protein(55. Frost et al., 2011) by Inhibiting DYRK1A mediated Tau phosphorylation reducing neurofibrillary tangles which are the identifying marker of Alzheimers disease. It is preventative to neurodegeneration and promotes neural health.

[Neurotoxicity and Adverse Drug Interactions]

All reference studies previously cited are dose dependent. Beta-Carbolines are helpful in small amounts and harmful in large amounts.

The beta carbolines from Banisteriopsis Caapi or Peganum Harmala combined with the antidepressant Prozac causes serotonin syndrome which has resulted in death in some cases.(56. Edinoff et al., 2021) It is considered unsafe during pregnancy because very large doses become toxic and will abort a human fetus.

Microdosing will safely reveal individual sensitivity. One or two breaths of smoke will safely reveal if eating *Peganum Harmala* will be a bad idea. Smoke rarely can cause nausea and only for a brief time. Eating it would be far worse in that case. *Peganum Harmala* is a Reversible MAOI, so it has fewer and less extreme reactions with medicine or food containing tyramine than a synthetic irreversible MAOI. A multivitamin containing fermented soy as an ingredient in an otherwise compatible diet can cause several hours of extreme nausea and vomiting. Some aged and smoked meats will be nauseating depending on the food processing methods. Fresh is always best due to tyramine from aged or damaged food being the primary cause of dietary incompatibility.

[Full Spectrum Alkaloids]

The alkaloids of *Peganum Harmala* seed are approximately 4-10% of the weight of the seed found in the brown skin of the seed, whereas the alkaloids of *Banisteriopsis Caap*i vine are only a fraction of 1% of the total weight of the vine found throughout the woody vine. Only those

Following are the most well-known, first discovered, and most largely present constituents:

The Beta-carboline alkaloids: harmine (initially known as - telepathine, yageine, banisterine), isoharmine, acetylnorharmine, norharmine, harmaline(aka dihydroharmine, DHH, harmidine), harmalol, harman(57. Pulpati et al., 2008), harmalacidine(HMC)(58. Wang et al., 2018), harmalidine and tetrahydroharmine(THH, leptaflorine)(59. Herraiz et al., 2010), isopeganine(60.

Asgarpanah & Ramezanloo, 2012), pegamine, dipeginol, dipegene(61. Faskhutdinov et al., 2000)

The Quinazoline alkaloids: desoxypeganine, deoxyvasicine (deoxypeganine), vasicine (peganine), vasicinone, peganidine, isopeganidine, dipegine

[Classifying the alkaloids]

Of the 160 known alkaloids found throughout the plant, beta-carbolines and their derivatives including the tetra-hydro-beta-carbolines (THBC) total approximately 60 of them. A sizable portion of the 100 remaining are pyrrolo-quinazoline alkaloids. In addition to their parent pyrroloquinazolines and quinazolines, exists a series of quinazoline glycosides also referred to as the glycoalkaloids.

The complete list of all 160 known alkaloids in *Peganum Harmala* was published in 2023 (62. Anstis et al., 2023), collectively presenting numerous recent discoveries about the known alkaloid contents. The molecular composition is being studied by the most cutting-edge techniques. Beyond chromatography and high performance liquid chromatography (HPLC), the newly discovered alkaloids structures, including stereochemistry, were elucidated through spectroscopic analyses, quantum chemistry calculations, and single-crystal X-ray diffraction in

2017 growing the list of known alkaloids found in *Peganum Harmala* in the past recent years.(63. Wang et al., 2018)

[Ayahuasca]

Peganum Harmala is often called "an amplifier" of entheogens. It has a synergistic effect with the 5HT neurotransmitters Psilocin, DMT, Bufotenine, and Mescaline caused by MAO enzyme inhibition delaying the metabolic process. *Banisteriopsis caapi* has the same primary alkaloids which are most abundant and therefore has mostly the same effect. Both plants can be used to make Ayahuasca. *Peganum Harmala* grows in arid desert conditions. *Banisteriopsis caapi* grows in the jungle as a vine. They contain the same primary alkaloids and are therefore both used for the purpose of creating Ayahuasca.

[Soma-Ayahuasca]

Peganum Harmala is most common in India, Algeria, Turkey, Iran, and Morocco where it is referred to as Harmel. There has been much debate about what the Soma Plant or Soma brew is that is mentioned in ancient Sanskrit texts and there is evidence suggestive that the plant could be *Peganum Harmala*.(64. Flattery & Schwartz, 1989) Zoroaster called it Haoma in the Avista Veda where it's considered the plant of life. It was called Soma by Brahma-manu in the Rig Veda. *Peganum Harmala* was found in Neolithic sites of the Caucasus from 5000 B.C. and in a pre-Dynastic Egyptian site dating back to 3700–3500 BC.(65. Samorini, 2019) Through

metabolic profiling of organic residues recovered from archeological artifacts it has been proven that *Peganum Harmala* was used for fumigation in Iron Age Arabia.(66. Huber et al., 2025)

Ayahuasca traditionally contains *Banisteriopsis Caapi* and Chacruna(*Psychotria viridus*). It is probable that "soma" was a term like "ayahuasca" where *Peganum Harmala* is used in place of Caapi in those dry regions. In Sanskrit, “soma” refers to a ritual drink. In Greek, the word “Soma” means “Whole Body” and this plant does have a whole-body effect.

[*Peganum Harmala* in Islam]

Peganum Harmala is known as Espand/Esfand in the Muslim community and is more culturally significant. It is mentioned in hadith literature to be consumed in a drink and in another place that burning the seeds is pleasing to the Jinn or angels and protects a person from “The Evil Eye” and that "God has appointed Angels over the plant", and in the Sahi’i medical collections of the 15th century it is written:

“Whoever for 40 days, eats 1 mesghal (4.64 grams) harmala mixed in water in every morning, the light of wisdom will turn on in his\her heart and he\she will be immune from 72 diseases that the least of them is leprosy.”

[Happiness]

Serotonin is a key neurotransmitter implicated in mood regulation and happiness. Increasing serotonin levels is the object of pharmaceutical antidepressants. Natural solutions for raising serotonin levels have also been established.(67. Young, 2007). *Peganum Harmala*, used solely for the purpose of an antidepressant has been the study focus of many research teams, and found to be effective,(42. Herraiz & Guillén, 2018) primarily by inhibition of the MAO Enzyme.

[Antidepressants]

The global antidepressants market size is approximately $20 billion USD in 2025. Recent data reveals a dramatic social increase in long-term prescriptions of antidepressants (68. Luo et al, 2020; 69. Mojtabai & Olfson, 2014).

MAOIs are medicine that inhibit MAO enzymes. Irreversible MAOIs are synthetic and not plant alkaloids. They are unnatural and far stronger than the reversible and natural MAOI. They covalently bond to MAO which permanently destroy it. Although once popular in medicine, today synthetic MAOIs are only used as a last resort for prescription antidepressants. During the 1950's, when synthetic MAOI antidepressants were first discovered, clinicians noted that they caused "inappropriate laughter". Over the years there were many deaths and near deaths as the full purpose and understanding of the MAO enzyme was only being first discovered. Variations of reuptake inhibitors became preferred antidepressant prescriptions for safety reasons and the MAOI earned a reputation as dangerous.

Now in 2026 the vastness of dietary and medicinal interactions documented in medical journals is mostly in reference to synthetic irreversible MAOIs and either does not apply to *Peganum Harmala* or it does apply to a far less degree. *Peganum Harmala* is a reversible MAOI which means that the beta carboline alkaloids have temporarily bonded, not covalently bonded to the MAO enzyme. Reversible natural MAOIs are much safer than synthetic irreversible MAOIs but rarely are the two types of MAOI differentiated by modern medical literature with warnings. Interaction risks with high-tyramine foods or with serotonergic drugs is possible but relatively uncommon in naturalistic and clinical settings.(70. Guimarães dos Santos & Hallak, 2025) Neurogenesis is now a recognized approach to antidepressant medication(71. Pascual-Brazo et al., 2014; 72. Rotheneichner et al., 2014) as more ideal solution than the currently popular reuptake inhibitors.

[Widescale misinformation]

At popular information sources such as WebMD, Drugs.com, and RxList in 2025 is published "Syrian Rue causes hallucinations" which is very misleading. Using 2 to 5g, with no other co-ingested visionary plants, *Peganum Harmala* will not cause any visions or hallucinations. 2g is minimally sufficient to provide medicinal action, any more than 4-5g of seeds by itself will cause nausea, not visions or hallucinations. Those information sources are incorrect, and the false information leads many away for fear of hallucinating.

[Materials and Methods]

Since 2018 SyrianRue.org has promoted collaboration with others who use or study Peganum harmala. Information sharing produced a wealth of practical information. In the United States Peganum Harmala is unregulated and not considered a controlled substance so it was openly discussed and used. Swallowing whole seeds with a glass of water is effective. Water based extracts are effective. Using a Food processor and a fine screen colander the brown skin of the seed can be separated from the white pit to capsule the powder which is also effective. All these methods use the full spectrum of alkaloids supplied by the seed as opposed to a select isolated beta-carboline alkaloid derived from synthesis or alkaloid isolations.

Also, regular inhalation of smoke multiple times per day was investigated. Various kinds of pipes were used. An issue being that almost half of the alkaloids melt and run eventually to clog a pipe or into the mouth. A pipe was devised to catch the oils so they can be smoked however all smoking devices were functional. Smoking only the brown skin of the seed and disposing of the pit increases quality.

[Smoke]

Smoking *Peganum Harmala* seed has a mild and comfortable effect that differs from the effect of eating it. All the alkaloids of interest exist on the brown skin on the seed. They melt and vaporize in heat. The seeds are prone to absorbing moisture as humidity, they should be fully dry with very low oven heat, if necessary, before smoking. A cigar torch lighter works best. Seed can be smoked in a pipe. Load a very small bowl. After one large breath, the charred and half burnt seeds should then be discarded rather than burning them further and reducing them

to white ash. Two good breaths will provide MAOI effect. The quality of the smoke is enhanced by discarding partly burned seed and not smoking the pit which contains no beta carboline alkaloids.

[Results and Discussion]

The investigation regarding regular use of the beta carbolines provided by 2 to 5 grams of *Peganum Harmala* seed worked out general dietary guidelines with some trial and error producing a strong takeaway that fresh food is generally safe and packaged food less so. Broth flavorings make an otherwise good plate of food incompatible with *Peganum Harmala*. The perceivable effect of 1 or 2 doses per day is subtle as the medicine works to do all that it does at the neurological level. A few people mentioned that things appear slightly brighter although the subtle effect at the cellular level and in metabolism of endogenous neurotransmitters is difficult to notice. Smoke inhalation provides an immediate mild and calming effect that is more perceivable and much shorter lasting in duration. For regular use, two serving of 2.5g is preferrable over 5g to most people. Large dose effects last 12 hours or more.

[Makes diet matter]

Peganum Harmala by itself is rarely credited for any great personal breakthroughs. In one exception, daily use of only *Peganum Harmala* after some months of reprise from other

unhealthy habits had one person claiming something of a personal transformation giving credit to *Peganum Harmala* alone. Foods with yeast extract preservatives or MSG cause nausea or digest poorly when mixed with *Peganum Harmala*, so does beer and wine. Diet and exercise are key to health and happiness - the ancient axiom remains. *Peganum Harmala* encourages healthy diet and will bring to the surface foods that are incompatible with it.

[Dietary Guidelines]

Certain foods are not good when mixed. For example, beer and milk. You can drink both beer and milk – but not at the same time. Don't suppose that you must give up beer because you drink milk every morning for breakfast. In a nutshell, this is the Ayahuasca or *Peganum Harmala* diet:

Avoid aged cheeses such as Parmesan, Chedder, Blue Cheese, Swiss, Gouda, Feta, Brie, Gruyere, and Emmental. Cheeses such as American cheese, Cottage Cheese, and fresh Ricotta are not aged and need not be avoided. Avoid aged, smoked or preserved meat such as Beef Jerky, Pepperoni, Mortadella, Salami, Shrimp paste, Pickled herrings, or salted Cod. Do not eat raw yeast, nutritional yeast, or any preservatives such as MSG which is a Yeast Extract. Do not eat fermented tofu or soy. Fermented soy is found in some vitamin supplements in large amounts.

The substance to avoid is tyramine. Very small amounts of tyramine will not make you nauseous, but large amounts will. Tyramine is poisonous to everyone, but the levels of tolerance to tyramine vary from person to person and from time to time. *Peganum Harmala* lowers tolerance for tyramine causing greater sensitivity to it. Tyramine is more commonly

found in old, mishandled, or damaged food because many food sources contain the beneficial amino acid tyrosine. Tyramine is created by bacteria that decarboxylate the tyrosine into tyramine.

You don't need to abstain from a dash of cinnamon or from *ALL* tree nuts to eliminate *ALL* tyramine from your diet when your body can metabolize a little. Brazil Nuts and hazel nuts are far worse than almonds. Avoid **large quantities** of spinach, cabbage, tomatoes, Italian flat romano beans(other beans are OK), pineapple, dates, snow peas, avocados, raw onion, eggplants, figs, beets, olives, broccoli, red plums, kim chee, prunes, raspberries, peanuts and peanut butter, Brazil nuts, walnuts, dried coconut flesh, (fresh sweet coconut water is OK), ginseng, licorice, cinnamon, anise, curry powder, most bullion broth cubes and powders, meat tenderizers, dry packaged and canned soups, gravy, sauces, stew mixes, instant soup dry powder bases, Soy and Teriyaki Sauce, hot paprika, nutmeg, brewer's yeast, fermented soy, beer and wine should be avoided.

Food that digests well with *Peganum Harmala*: Fresh chicken, eggs, fresh fish, fresh beef, white bread, wheat bread, rye bread, English muffins, crackers, bagels, hot and cold cereal, cream of wheat, rice, cooked dried beans, peas, and lentils, all pasta, apple, banana, mangoes, blueberries, melons, melon blossoms, egg noodles, rice, corn, asparagus, carrots, pumpkin, squash, zucchini, cooked onion, bread fruit, american cheese, ricotta, cottage cheese, cream cheese, eggs, most canned salmon or tuna fish, tuna salad, milk: whole, 2% or skim, salt, chives, sugar, maple syrup, honey, and salad dressing made from olive oil and lemon juice. Baby kale

can be cooked or in a salad with hibiscus flowers. Potatoes, sweet potatoes, yams, yucca, and breadfruit are all good. Pistachios, cashews, and almonds are ok in small quantity although they have trace amounts of tyramine. Bananas are good with attention to remove all banana peel strings because they contain tyramine.

[Additional Observations]

Peganum Harmala seed glows extremely bright under a standard UV blacklight, however only when mixed with water. Soak seeds in a glass for a few days, then pour the glass in a slow-moving stream with a blacklight at night to see a long bright fluorescent streak in the water. Caapi also glows. Yellow Caapi glows brighter than Red Caapi, and red glows more than Black Caapi. Urine excreted after metabolizing Rue or Caapi also glows very bright so keep an ultraviolet blacklight handy to check it out. The pure alkaloids glow, however most brightly when wet.

[Conclusion]

Promising preclinical evidence suggests that it could be preventative for Alzheimer's and neurodegeneration. Evidence also suggests that it could be preventative for cancer because it is a growth inhibitor for cancer. It can be part of an herbal treatment for depression. The beta-carbolines in *Peganum Harmala* influence cellular proliferation body-wide. Evidence suggests it can be used as an approach to create new bone cells or improve osteoporosis conditions and that it could be preventative to such conditions. Evidence suggests that beta-carboline induced

beta cell production could accompany stem cell applications. Evidence suggests that *Peganum Harmala* can accompany clinical psilocin to increase effectiveness.

[Author Contributions]

History of this research:

The first research publication by Brian Aberle at ResearchGate.net in 2016 titled:

Proper *Peganum Harmala* usage for increased serotonergic transmission

Followed by:

Neurodegenerative Diseases in 2018 also at ResearchGate

Followed by:

The initial loadbearing section of this version published as draft preprint Aug 2023 at

ResearchGate.net DOI: 10.13140/RG.2.2.28588.23686

[Competing Interests]

The author declares no competing interests. No funding was received to conduct this research.

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