RESEARCH PAPER

Rasayana Alkaloids in Aging Modulation: Mechanistic Insights from Tinospora cordifolia and Tribulus terrestris

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ABSTRACT
As people age, older cells accumulate damage in their DNA and older cells and pathways become disrupted from evolution, making them more vulnerable to many chronic diseases. In Ayurvedic medicine, rasayana therapy is thought to combat the consequences of aging. In this review we aim to highlight the phytochemistry and pharmacological potential of alkaloids of Rasayana preparations such as Tribulus terrestris, Tinospora cordifolia and Phyllanthus emblica. The literature has been retrieved from different scientific databases giving particular emphasis on phytochemical and pharmacological aspects of the mechanism of aging. The selected herbs contain a rich amount of bioactive alkaloids like berberine, palmatine, magnoflorine, and beta-carboline derivatives. These compounds have been found to be antioxidant, anti-inflammatory and metabolic-modulatory. The existing evidence from in vitro and in vivo studies on the selected compounds in the Rasayana formulations, indicates the involvement of these compounds in the regulation of evolutionarily conserved longevity pathways. While there is limited evidence of lifespan extension, the available data suggest the possibility that alkaloids obtained from Rasayana therapy could be used in the context of increasing the cellular stress resistance and maintaining metabolic homeostasis.
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INTRODUCTION

An aging population is a major public health challenge throughout the world. The World Health Organization estimates that by 2030 there will be about 1.4 billion and by 2050, 2.1 billion people over 60 years of age. The shift is linked with an increase in the incidence of age-related tissue and organ damage, which raises the likelihood of developing chronic diseases like cardiovascular diseases, Alzheimer's disease (AD), and osteoporosis. Model organisms like *Caenorhabditis elegans*, mice, rats, zebrafish (Danio rerio) and Drosophila melanogaster have been important in the experimental study of mechanisms of aging in recent years [1].

Aging is a biological process that happens to everyone, is inevitable and cannot be slowed down or avoided, and is associated with a progressive decline in functional properties of cells, tissues and organs. The reduction causes a deterioration of homeostasis and adaptability to internal and external stressors [2]. Some age-related changes like wrinkles and diminished hair pigmentation are not life threatening, however the process is much more than it is cosmetic – it impacts the physiological integrity as well. At the molecular level, increased levels of ROS cause oxidative stress and cause damage to cells macromolecules, which disrupts proteostatic degradation processes such as autophagy and proteasome mediated degradation. In addition, the errors in the process of transcription and translation, as well as disturbances in mechanisms of molecular chaperone protein folding contribute to cell dysfunction [4, 5] .While drugs continue to be the mainstay of disease treatment, there are no clear treatments that are known to prevent or cure aging-related diseases. Therefore, measures taken to prevent the occurrence of these diseases are becoming important and are in great focus, especially some nutritional and phytochemical measures. The use of bioactive compounds from plants has been investigated for their beneficial roles in reducing aging and its related chronic diseases to a large extent [6].

The nourishment and optimum transport of nutrients in the body is called rasayana (rasa + ayana). It is thought to increase the purity of rasa (nutrient essence), which would lead to better health, longevity, cognitive function, immunity, physiological strength, youthfulness, complexion and sensory functions[7,8].Rasayana Churna (RC) is a classical ayurvedic poly herbal formulation made up of equal quantity of dried stem of *Tinospora cordifolia* (Guduchi), dried fruit of *Tribulus terrestris* (Gokshura) and dried pericarp of *Phyllanthus emblica* (Amla). According to Ayurvedic literature, this formulation is a powerful rejuvenator for improved vitality, immunity and longevity and is also an adaptogen[9]. These botanicals have been subjected to phytochemical analysis and numerous bioactive compounds have been identified, such as polyphenols, flavonoids, tannins, saponins, and alkaloids [10].

Alkaloids, in particular, are of interest because they have a range of well-studied pharmacological activities, clear molecular targets and the capacity to modulate important biological pathways involved in oxidative stress, inflammation, antimicrobial defense, and cancer progression[11]. The isoquinoline alkaloids found in *T. cordifolia* and other Rasayana herbs, like berberine, palmatine, and magnoflorine, have been shown to possess antioxidant, immunomodulatory and anticancer properties in vitro and in vivo studies[12,13].

Recent evidence also implicates these alkaloids in the modulation of evolutionary conserved pathways related to aging and longevity such as insulin/IGF-1 signaling, AMP-activated protein kinase (AMPK), mechanistic target of rapamycin (mTOR) and FOXO transcription factors. They control cellular stress responses, metabolism, and lifespan in different model systems, such as C. elegans. Hence, in the present review, the focus will be on the pharmacological importance of alkaloids as important phytochemical constituents of Rasayana Churna. This review attempts to draw conclusions about their mechanistic functions in aging associated pathways and their possible roles in longevity research by incorporating results from in vitro, in vivo and model organism studies.

METHODOLOGY

The review article was developed through an extensive literature search of reputable databases including PubMed, Google Scholar, and Science Direct focusing on keywords such as “pharmacology,” “phytochemistry,” “alkaloids in *Tinospora cordifolia*,” “*Tribulus terrestris*,” and “*Phyllanthus emblica*.” The search included original research articles, review articles and books published between 1956 and 2024, with emphasis on peer-reviewed and validated sources. Experimental evidence related to *Tinospora cordifolia*, *Tribulus terrestris*, and *Phyllanthus emblica* was systematically collected, screened based on inclusion and exclusion criteria, and critically analyzed to support the comprehensive nature of this review.

Study selection and eligibility criteria

Studies investigating Rasayana-derived alkaloids and their pharmacological effects relevant to aging and longevity were included, including in vitro, in vivo and clinical studies. Only studies with full text available were included. Manual screening of reference lists of selected articles was performed to identify additional relevant studies. All eligible studies were included in the final analysis.

Rasayana Churna: Preparation and Benefits

Rasayana churna is a classical Ayurvedic polyherbal formulation comprising equal proportions of *Tinospora cordifolia* (Guduchi), *Tribulus terrestris* (Gokshur), and *Phyllanthus emblica* (Amla), traditionally indicated for promoting systemic homeostasis, vitality, and longevity[14].The formulation exhibits diverse pharmacological potential attributed to its rich phytochemical composition, including alkaloids, flavonoids, saponins, phenolics, and polysaccharides[15].

Tinospora cordifolia is extensively characterized for its immunomodulatory activity, mediated by bioactive constituents that regulate macrophage function, cytokine production, and key signaling pathways such as NF-κB and interleukin-mediated responses [16,17]. Experimental and clinical studies further demonstrate its role in metabolic regulation, hepatoprotection, and protection against oxidative stress–associated disorders [18].*Tribulus terrestris* exhibits antimicrobial, anti-inflammatory, and cytotoxic properties, primarily attributed to steroidal saponins, flavonoids and alkaloids with reported pro-apoptotic activity in cancer models [19]. *Phyllanthus emblica*, a rich source of ascorbic acid and polyphenols, contributes to redox balance, immune regulation, and inhibition of cellular proliferation through modulation of oxidative and inflammatory pathways [20].

The pharmacological efficacy of Rasayana churna can be attributed to the synergistic interaction of its constituent phytochemicals, which collectively influence multiple molecular targets involved in inflammation, cellular survival, and immune regulation. Such multi-target activity aligns with the concept of polyherbal synergy and systems pharmacology, where combined bioactives enhance therapeutic outcomes and biological resilience [21].

Overall, Rasayana churna demonstrates integrated immunomodulatory, cytoprotective, antimicrobial, and antiproliferative effects. Among its phytoconstituents, alkaloids represent a critical class due to their role in signaling pathway modulation and therapeutic activity, warranting focused investigation to elucidate their mechanistic contributions

Alkaloid Profile of Selected Rasayana Plants

Alkaloids are a diverse class of nitrogen-containing compounds derived from plant, microbial, and animal sources. They are classified into multiple subclasses based on their heterocyclic structures and biosynthetic origins, including tropanes, indoles, imidazolines, piperidines, isoquinolines, pyrrolizidines, quinolizidines, and pyrrolidinyl alkaloids [22,23].

Historically, alkaloids have exhibited both toxic and therapeutic properties, with several compounds being utilized as antipyretics, analgesics, and antidotes [24,25]. Despite concerns regarding toxicity, alkaloids have shown significant potential in drug development due to their wide-ranging pharmacological activities, including antioxidant, anti-inflammatory, antibacterial, antispasmodic, anticancer, antihypertensive, and central nervous system-modulating effects[23,26].Notably, a substantial number of alkaloids have demonstrated anti-aging properties in experimental studies[27].

Tinospora cordifolia contains a diverse array of alkaloids, primarily belonging to isoquinoline and aporphine classes. Major constituents include berberine, palmatine, jatrorrhizine, magnoflorine, and corydine [28].These compounds are mainly derived from isoquinoline biosynthetic pathways and are structurally classified as protoberberines, which represent the predominant alkaloid fraction in this plant [29].

Tribulus terrestris is reported to contain β-carboline alkaloids such as harmane and norharmane, along with minor alkaloidal constituents [30]. These indole-derived compounds contribute to the plant's pharmacological profile, complementing its major saponin content[31,32].

Phyllanthus emblica, although primarily characterized by high vitamin C and phenolic content, also contains minor amounts of nitrogenous compounds [33]. Constituents such as phyllantine and related compounds have been identified as part of its phytochemical profile [34].

The presence of structurally diverse alkaloids across these Rasayana botanicals contributes to their broad pharmacological spectrum. These include protoberberine alkaloids in *T. cordifolia*, β-carboline alkaloids in *Tribulus terrestris*, and lignan-related compounds in *Phyllanthus emblica*, reflecting distinct biosynthetic origins and therapeutic potentials. Collectively, these compounds support the traditional use of Rasayana formulations in managing oxidative stress-related disorders and promoting overall health.

Mechanistic Insights Relevant to Aging and Longevity

An integrated network of evolutionarily conserved signaling pathways governing cellular homeostasis, metabolic balance, and stress adaptation underlies the genetics of aging. These pathways all act on and converge towards common processes including, redox state, nutrient sensing, proteostasis and immune signaling that ultimately determine lifespan and healthspan. This functional interdependence allows them to cooperate in responding to environmental and metabolic signals.

1. **Redox Homeostasis and Cytoprotective Stress Responses**

Reactive oxygen species (ROS) are mainly produced during mitochondrial respiration and act both as signaling mediators and mediators of cellular damage. Although high levels of ROS cause oxidative damage to proteins, lipids and DNA, lower doses of ROS induce adaptive stress responses that promote cellular resilience (mitohormesis). Redox balance is sustained by the antioxidant system including superoxide dismutase, catalase, and peroxiredoxins [38].

Several cytoprotective pathways, such as Nrf2-mediated antioxidant responses, heat shock proteins and unfolded protein responses are crucial to maintain proteostasis as well cellular integrity. Although these pathways are activated by energy deprivation, they also lead to increased resistance against stress-induced damage and extended longevity [45].

2. **Nutrient-Sensing Pathways: IIS, mTOR, and AMPK**

Nutrient-sensing pathways form a key regulatory axis of aging. The Insulin/IGF-1 Signaling (IIS) pathway is a key regulator of metabolism, growth and lifespan; decreased IIS activity has been consistently linked to longevity in all species studied [36,37]. In model organisms like Caenorhabditis elegans, IIS attenuation promotes the activation of downstream transcriptional programs associated with stress resistance and survival [37].

Mechanistic target of rapamycin (mTOR) is a central node for integrating environmental nutrient availability and cellular energy state to control anabolic and catabolic processes. mTOR complex 1 (mTORC1) promotes biosynthesis and inhibits autophagy while its inhibition shifts cellular function toward maintenance and repair.

AMP-activated protein kinase (AMPK) serves as an energy sensor in the cell, balancing IIS and mTOR signaling. AMPK activation stimulates catabolism, improves mitochondrial function and contributes to metabolic homeostasis [42].

3. **FOXO Transcription Factors**

FOXO transcription factors act as central integrators of longevity signaling and orchestrate many protective pathways [38–41]. When IIS is low, FOXOs become activated to regulate antioxidant defense genes, genes involved in DNA repair, apoptosis, and autophagy [38–40]. A genetic variant in FOXO3 has previously been robustly linked to increased human lifespan [41].

4. **Epigenetic and Non-coding RNA Regulation**

DNA methylation and histone modifications are epigenetic mechanisms that regulate gene expression programs related to aging (45). Moreover, they specify non-coding RNAs, for example, microRNAs and long non-coding RNAs, which additionally mediate post-transcriptional regulation and cellular adaptation. These regulatory systems interplay together with nutrient-sensing pathways and impacts metabolic function and stress responses [37].

5. **Autophagy and Proteostasis**

Autophagy is a conserved protein and organelle degradation pathway that serves to remove dysfunctional components of the cell. Regulated by nutrient-sensing pathways, mTOR and AMPK. Ablation of the senescent cell phenotype combined with increased autophagy stimulates cellular quality control, prevents the accumulation of misfolded and aggregated protein aggregates and support mitochondrial function [43,44].

6. **Inflammation and Immune Signaling**

Chronic low-grade inflammation ("inflammaging") is a hallmark of aging and a major driver of age-related pathology .Key regulators such as NF-κB and mTOR promote the expression of pro-inflammatory mediators, whereas AMPK exerts anti-inflammatory effects. Persistent inflammatory activation disrupts tissue homeostasis and accelerates functional decline [46]. Therefore, aging is governed by interconnected pathways controlling nutrient sensing, redox balance, proteostasis, and immune signaling [35-46]. Rasayana-derived alkaloids may modulate key nodes within this network, supporting longevity and mitigating age-related decline [37-44].

Rasayana Botanicals and Their Relevance to Aging Modulation

Rasayana formulation traditionally consists of three major botanicals: the stem of Guduchi *(Tinospora cordifolia)*, the fruit of Gokshur (*Tribulus terrestris)*, and the fruit of (Amla) *Phyllanthus emblica* , which have a wide spectrum of therapeutic action.

A) Experimental Evidence of Guduchi *(Tinospora cordifolia)* Alkaloids in Aging-Associated Biological Mechanisms

Overview of Guduchi *(Tinospora cordifolia)* and its Alkaloid Constituents

Tinospora cordifolia (Thunb.) Miers (Guduchi), a member of the family Menispermaceae, which has been widely used as an Ayurvedic Rasayana drug having properties to prolong life, assisting in immunity and resisting stress [47–49]. It is a climbing shrub that grows throughout the tropical regions of the Indian subcontinent and other areas of Asia and Africa [50–54].

Phytochemical studies have identified a broad spectrum of bioactive constituents in *T. cordifolia*, including alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoids, phenolics and polysaccharides (55-57). Thus, among these, alkaloids especially the protoberberine and aporphine types are regarded as major contributors to its pharmacological actions. Berberine, palmatine, magnoflorine, jatrorrhizine, tembetarine and corydine[58-63] are the major identified alkaloids.

These alkaloids are well known for their biological effects such as antioxidant, anti-inflammatory, antidiabetic, neuroprotective and immunomodulatory activities all of which may be relevant to the modulation of age-associated cellular processes.

A: Whole plant **B: Fruit** **C: Leaves** **D: Flower**

Figure 1: Images of parts of Guduchi *(Tinospora cordifolia)* **https://www.inaturalist.org/observations/321173165**

Table 1. Summary of experimental evidence on alkaloids from Guduchi in aging-associated biological mechanisms

Sr no.	**Phytochemical**	**Experimental Model**	**Chemical class**	**Parameters**	**Relevance to Aging**	**Mechanism**	**Geroprotective Potential**	**Reference**
1	Magnoflorine	*Caenorhabditis elegans*	Aporphine alkaloid	Antioxidant activity DPPH, ABTS radical scavenging; AChE/BChE inhibition	↑ Antioxidant activity; cholinesterase inhibition	Free radical scavenging; AChE/BChE inhibition	Antioxidant, neuroprotective effects	64
	Magnoflorine	Mouse model of non-alcoholic fatty liver disease (NAFLD)	Aporphine alkaloid	Lipid profile, autophagy-related proteins (Parkin, PINK1), inflammation markers (NLRP3 inflammasome components, IL-1β)	↓ROS; ↑ Improved lipid metabolism ↓ Hepatic inflammation	Parkin/PINK1-mediated mitophagy activation	Anti inflammatory, Antioxidant	65
2	Berberine	*Caenorhabditis elegans*	Protoberberine alkaloid	Lipid accumulation	↓ lipid accumulation	AMP-activated protein kinase (AMPK) activation	Metabolic regulation, Potential anti-aging	66

	Berberine	*Caenorhabditis elegans*	Protoberberine alkaloid	Lifespan assay; locomotion; oxidative stress markers	↑ lifespan; ↑ locomotor activity; ↓ ROS	AMPK activation; mTOR inhibition; SIRT1/FOXO & Nrf2 upregulation; NF-κB suppression	Anti-aging, Antioxidant, Anti-inflammatory	67
3	Palmatine	*Caenorhabditis elegans Aβ-induced neurotoxicity model*	Protoberberine alkaloid	Paralysis delay; ROS measuremen; antioxidant enzyme activity assays (SOD, CAT)	Delayed paralysis; ↓ Aβ aggregation; ↓ ROS; ↑ SOD/CAT	HSF-1-dependent sHSP upregulation	Neuroprotection, Stress resistance,	68
	Palmatine	Rat	Protoberberine alkaloid	DPPH, NO, H_2O_2; lipid peroxidation; AGEs; CAT, SOD, glutathione peroxidase (GPx)	↓ ROS & ↓ AGEs; ↑ antioxidant enzymes	Reactive oxygen species and reactive carbonyl scavenging; enhanced antioxidant defense	Anti-oxidant, Antiglycation	69
4	Jatrorrhizine	PC12 cells (H_2O_2-induced injury)	Bisbenzylisoquinoline alkaloid	Cell viability, antioxidant enzymes (SOD, HO-1), ROS levels, MDA, LDH, Mitochondrial membrane potential (MMP), caspase-3	↑ Cell viability ; ↑ Antioxidant enzyme activity (SOD, HO-1) ↓ ROS, MDA, LDH release ; Preserved MMP (mitochondrial health) ; ↓ apoptosis	Enhancement of antioxidant defense enzymes (SOD and HO-1) ; mitochondrial protection	Anti-oxidant, Neuroprotective	70
5	Tembetarine	In vitro cytotoxicity model	Alkaloid	Cell viability	↑ cell viability; Low cytotoxicity	Antioxidant-mediated cytoprotection	Antioxidant Antibacterial	71

Compound-Specific Evidence Of Guduchi *(Tinospora Cordifolia)* Alkaloids In Aging-Associated Biological Mechanisms

Magnoflorine

Magnoflorine is a potent antioxidant, possesses enzyme inhibitory activities and reduces oxidative stress and modulates metabolic processes. It is demonstrated to have a free radical scavenging activity and inhibits acetylcholinesterase, butyrylcholinesterase and α-glycosidase enzymes which are linked with advanced age-related diseases. Magnoflorine exerts neuroprotection via PINK1/Parkin-mediated mitophagy activation and simultaneously inhibiting the NLRP3 inflammasome. These effects aid in the maintenance of cellular homeostasis by promoting mitophagy and decreasing inflammation. These mechanisms are correlated with improved stress resistance and lifespan extension in model organisms such as C. elegans[64,65].

Berberine

Berberine, one of the most well-studied isoquinoline alkaloids, has been shown to exert strong effects on lipid metabolism and energy homeostasis. Here, we demonstrate that berberine inhibited lipid accumulation and modulated genes components of the metabolic pathways in C.elegans. AMPK Activation as a Mechanism for Mediating these Effects Activation of metabolic homeostasis through AMPK has been closely linked to lifespan regulation, speculating the involvement of berberine on longevity-related processes[66-67].

Jatrorrhizine

We found that Jatrorrhizine had strong neuroprotective activity against cell injury induced by oxidative stress. It has been reported in experimental models that it lowers ROS levels, diminishes lipid peroxidation and improves the endogenous antioxidant defenses; such as superoxide dismutase (SOD) and heme oxygenase-1 (HO-1). Moreover, jatrorrhizine prevents mitochondrial dysfunction by preserving mitochondrial membrane potential and inhibiting apoptosis through suppression of caspase-3 activation. These cytoprotective actions underline its potential protective mechanism in promoting neuronal survival and maintaining cell viability during an oxidative stress item typical of aging [68].

Palmatine

Palmatine displays powerful antioxidant and anti-glycation properties that help alleviate oxidative and proteotoxic stress. Is has been proved to improve the function of antioxidants enzymes like catalase, super oxide dismutase and glutathione peroxidaze.

Palmatine decreases levels of ROS, extends the lifespan in C. elegans models of amyloid-β-induced toxicity, and upregulates several categories of stress-responsive genes such as sod-3. It also promotes expression of HSF-1 regulated heat shock proteins, which help maintain proteostasis and limit protein aggregation. Palmatine improves the cellular stress resistance, but it does not essentially lengthen lifespan in normal condition [69,70]; however, the promotion of healthspan seems more reasonable.

Tembetarine

Antioxidant and antibacterial activities of Tembetarine for improving cellular stress responses It may improve resistance to stressors associated with ageing, by decreasing oxidative damage and maintaining cellular homeostasis. Although still very limited in longevity models, the biological activities of quercetin imply that modulation of multiple cellular processes implicated in aging merits further inspection [71].

B) Experimental Evidence of Gokshur (*Tribulus terrestris*) Alkaloids in Aging-Associated Biological Mechanisms

Overview of *Gokshur (Tribulus terrestris)* and Its Alkaloid Constituents

Tribulus terrestris L. of the Zygophyllaceae family commonly known as Gokshura or Chavhal is an ancient herb used in Ayurveda and an important medicinal plant characterized for its steroidal, anti-atherogenic activity. Tribulus is derived from the Greek word Tribolos, which translates as spiny fruit. The species is very widely distributed in the tropics and subtropics of the world, including India, China, Africa, Australia (Queensland), southern USA (Florida), Mexico, Spain, and Bulgaria. It belongs to the family Zygophyllaceae, which contains about 25 genres and around 250 species including *Tribulus terrestris*, *Tribulus cistoides* and *Tribulus alatus* [72-73].

T. terrestris has hirsute, silky hairs and is a low-growing herb, usually prostrate in form 10–60 cm in height. It forms a tap root system and can also behave as a summer annual in variable environmental systems [74]. The fruits are unique, spinous or tuberculate. The pods of these plants contain sharp spines that aid in dispersal by sticking to animals and human clothes [75].

T. terrestris is rarely used as a tonic, aphrodisiac, diuretic (293), antihypertensive, and urinary tract medicine for the treatment of genitourinary disorders. Results of Phytochemical Studies revealed the existence of steroidal saponins (dioscin, protodioscin and tribestin), flavonoids (quercetin & kaempferol derivatives), phytosterols such as β-sitosterol, stigmasterol and campesterol[[76-82].

Furthermore, the plant also contains β-carboline and indole alkaloids such as harman, harmine, harmalol, tribulusamide C, tribulusterine and tribulusin mainly localised in the fruits while harmaline is reported from head stems of leaves [14]. [83-87]

These alkaloids, although less abundant than saponins, are significant for their role in cellular signalling and stress-response pathways associated with the modulation of aging and disease.

A: Whole plant B: Fruit C: Flower

Figure 2. Images of parts of ***Gokshur (Tribulus terrestris)*** https://www.inaturalist.org/observations/338108465

Table 2. Summary of Experimental Evidence on Alkaloids from *Gokshur (Tribulus terrestris)* in Aging-Associated Biological Mechanisms

Sr no.	Phytochemical	Experimental Model	Chemical class	Parameter	Relevance to Aging	Mechanism	Geroprotective Potential	Reference
1	Harmane	*Caenorhabditis elegans*	β-Carboline alkaloid	Lifespan under infection	↑ Lifespan during infection	Stimulates innate immune response via gene F35E12.5	Immunomodulatory, infection resilience	88
	Harmane	*Leishmania* infantum (parasite) + human monocytes	β-Carboline alkaloid	Parasite proliferation; PKC activity; cell cycle	↓ Parasite growth; cell cycle arrest	DNA intercalation	Antiparasitic	89
	Harmane	Rat hepatic microsomes	β-Carboline alkaloid	Lipid peroxidation assay	↓ lipid peroxidation	Free radical scavenging	Antioxidant	90
	Harmane	Mouse	β-Carboline alkaloid	Forced swim test	↓ Immobility time	Benzodiazepine receptor modulation; ↑ monoamine neurotransmitters	Neurobehavioral modulation	91
2	Harmine	Streptozotocin-induced diabetic rats	β-Carboline alkaloid	Testicular histopathology ; Apoptotic index (TUNEL assay) ; Serum sex hormones	↓ Testicular oxidative damage; ↓ apoptosis; ↑ Testosterone, LH, FSH	Antioxidant action reduces lipid peroxidation and NO; Anti-apoptotic effect preserves testicular function;	Reproductive aging protection	92
	Harmine	Parkinson's mouse model	β-Carboline	Motor function tests (pole	↑ Motor performan	Microglial suppression;	Neuroprotective, antioxidant	93

			alkaloid	test, open field); dopamine levels; ROS ; histopathology of substantia nigra	ce and dopamine; ↓ Oxidative stress; ↓ microglial activation	antioxidant activity		
	Harmine	human cancer cell lines; mouse tumor models	β-Carboline alkaloid	Tumor volume ; IC50 in cancer cell lines; cell cycle analysis	↓ Tumor growth; cell cycle arrest ; synergism with chemotherapy	DNA intercalation; PI3K/Akt, NF-κB inhibition ;	Anticancer	89
	Harmine	Leishmania parasite + human monocytes	β-Carboline alkaloid	IC50 for parasite growth inhibition; PKC activity assay ; Cell cycle analysis	↓ Parasite proliferation; Cell cycle arrest	DNA intercalation; PKC inhibition	Antiparasitic	94
	Harmine	Bacteria and fungi	β-Carboline alkaloid	Minimal inhibitory concentration (MIC)	↑ Antimicrobial activity	Enzyme & cell structure disruption	Antimicrobial	95
3	Harmaline	Male Swiss mice	β-Carboline alkaloid	Elevated plus maze (anxiety-related behavior) ; Locomotor activity	Low dose anxiogenic ; high dose anxiolytic; ↓ locomotion	Olivocerebellar and benzodiazepine receptor modulation	Neurobehavioral modulation	96
	Harmaline	Ovarian cancer cells	β-Carboline alkaloid	Cell viability (MTT) ; Apoptosis; ROS	↓ viability (IC50 ~300 µM), ↑ ROS-mediated apoptosis	ROS-mediated apoptosis; metastasis suppression	Anticancer, Pro-oxidant	97
	Harmaline	Human hepatoma HepG2 cells; Guinea pig hepatic cytosol	β-Carboline alkaloid	CYP1A1 activity	↓ Carcinogen activation	AhR inhibition; Ubiquitin-proteasomal degradation	Chemopreventive	98
4	Harmalol	Mice, PC12 cells	β-Carboline	ROS levels, Mitochondrial function	↓ oxidative stress; Neuronal protection	ROS scavenging; MAO inhibition;	Neuroprotective, antioxidant	99

			alkaloid	; Apoptosis assays		mitochondrial protection		
	Harmalol	Dog ,Rat heart	β-Carboline alkaloid	Heart rate ; Blood pressure ; Myocardial contractility	↓ Heart rate (bradycardia reduction) ↑ Myocardial force	Direct cardiac modulation	Cardiovascular modulator	100

Compound-Specific Evidence of *Gokshur (Tribulus terrestris)* Alkaloids in Aging-Associated Biological Mechanisms

The summarized evidence highlights key experimental findings, while the following subsections describe the aging-related biological activities of major phytochemicals from *Gokshur (Tribulus terrestris)*

Harmane

Harmane has been identified as a survival enhancer in C. elegans, specifically under conditions of pathogenic stress [5]. What is most interesting this effect seems to be mediated through activation of immune pathway and not direct antimicrobial activity. Experimental evidence shows that harmane upregulates immune effector genes including F35E12. 5, possibly via modulation of stress-responsive signaling pathways such as p38 MAPK. Its mechanism of action seems not dependent on the insulin/IGF-1 signaling pathway, implying an alternative organismal resiliency pathway. It also inhibits lipid peroxidation and so even supports antioxidant properties in combating age related oxidative stress [88-91].

Harmine

Harmine shows significant antioxidant and anti-inflammatory effects in stabilizing the homeostasis of affected cells. Saccharin Controlled Translation Sacharoma at Mitoliberator It has been shown to increase antioxidant defenses, decrease lipid peroxidation, and inhibit proinflammatory mediators of nitric oxide and cyclooxygenase-2.

Moreover, harmine is reported to have mediated mitochondrial functions and genomic stability by regulating DNA repair factors. It also has a crucial role in modulation of major signaling pathways promoting cell survival and metabolism, particularly inhibiting apoptosis under stress conditions. These effects overlap with conserved pathways associated with longevity, such as those regulating oxidative stress response and metabolic homeostasis, which suggest its utilization in increasing healthspan[89,92-95].

Harmaline

Only harmaline showed substantial activity in this domain which modulate cellular stress responses and apoptosis. It modulate the pathway by controlling ROS levels and stimulates signaling molecules like p53, Bax involved in oxidative stress.

Moreover, it inhibits matrix metalloproteinases, suggesting its role in the preservation of tissue integrity. In addition to altering stress hormone levels, its interactions with central nervous system pathways and intracellular signalling cascades imply global regulatory roles in organismal stress adaptation. These mechanisms suggest it may play a role in increasing cellular adaptability and/or maintaining homeostasis during stressors associated with aging [96, 97, 98].

Harmalol

Harmalol is a β-carboline alkaloid that plays a role in antioxidant defense and mitochondrial protection. It was demonstrated to contribute to lowering markers of oxidative stress, maintaining mitochondrial function, and modulating important enzymatic systems associated with cell metabolism.

Slightly, harmalol affects the detoxification pathways as well either by inhibiting xenobiotic-activating enzymes like CYP1A1 limiting the damage of toxic compounds in the cells. Importantly, they are all functionally linked to enhancement of stress resistance and metabolic homeostasis, two essential features of aging and longevity [99,100].

C) Experimental Evidence of Amla *(Phyllanthus emblica)* in Aging-Associated Biological Mechanisms

Overview of Amla *(Phyllanthus emblica)*

Amla or Indian gooseberry (*Phyllanthus emblica L.*) is a medicinal plant species in the family Euphorbiaceae and it is regarded as one of the most valuable and important herbs in traditional Ayurvedic and Unani systems of medicine for various ailments, lesquels [101,102]. According to Indian mythology, it is one of the oldest plants that were originated, indicative to its age-long cultural and medicinal value.

Widely distributed in tropical and subtropical regions of Pakistan, Uzbekistan, Sri Lanka, Southeast Asia, China and Malaysia. Genus *Phyllanthus* which includes 550–750 species divided into numerous subgenera [103].

P. emblica is a small to medium sized deciduous tree of 8-18 m height with thin, light grey exfoliable bark in small flakes. Leaves are simple, subsessile and closely arranged on the branchlets to give a pinnate appearance. The flowers are unisexual, yellowish-green in fascicles, the fruits glabous and globose-shaped on a pericarp covered with pale yellow flesh and six vertical ridges along which the glabs, trigonous seeds lie [104].

P. emblica fruit is among the richest natural sources of ascorbic acid (vitamin C), which represents the most abundant bioactive component in *P. emblica* fruit It also contains a number of phytochemicals, such as alkaloids, phenolics, tannins, flavonoids, saponins, terpenoids, fixed oils and essential oils [8], amino acids and minerals. We also have fatty acids: linolenic, linoleic, oleic, stearic, palmitic and myristic. Important tannins are represented by emblicanin A, emblicanin B, pedunculagin and punigluconin. Other important components occur such as gallic acid, amlaic acid, astragallin, β-carotene, β-sitosterol,[105-109] chebulagic acid and/or chebulic acid[104] quercetin and rutin.

While *P. emblica* is renowned mainly for its large content of vitamin C and polyphenols, a variety of minor alkaloidal and nitrogen compounds enhances the pharmacological profile. It contains various phytochemicals, which are responsible for its antioxidant, immunomodulatory and cytoprotective effects in relation to aging and longevity.

A: Leaves **B: Whole plant** **C: Fruit**

Figure 3. Images of parts of **Amla *(Phyllanthus emblica)***(https://www.inaturalist.org/observations/299165924)

Table 3. Summary of Experimental Evidence on Amla *(Phyllanthus emblica)* in Aging-Associated Biological Mechanisms

Phytochemical	Experimental Model	Parameter	Relevance to Aging	Mechanism	Geroprotective Potential	Reference
Phyllanthus emblica (Amla)	Caenorhabditis elegans	Lifespan ; Antioxidant assays ; Cholinesterase inhibition ; Thermotolerance	↑Antioxidant capacity; ↓ Acetylcholinesterase (AChE) activity; ↑ Thermal resistance; lifespan extended by ~18.5%	Free radical scavenging; cholinesterase inhibition ; antioxidant enzyme upregulation	Lifespan extension, Antioxidant, Neuroprotective	110
Phyllanthus emblica (Amla)	Drosophila melanogaster	Lifespan; Mating behavior ; Fertility; Development time	↑ Lifespan ; ↑ sexual behavior ↑ reproductive fitness and vitality	Adaptogenic effects ; improve vitality and reproductive function, possibly via stress-response modulation	Longevity, Reproductive health, Vitality enhancement	111
Phyllanthus emblica (Amla)	Rat	Preneoplastic lesion counts ; cell proliferation (PCNA); antioxidant enzymes;	↓ Preneoplastic lesions and proliferation ; ↓ ROS/NO; ↓ mutagenicity	ROS scavenging ; enhancement of antioxidant defenses ; DNA protection	Chemopreventive, Antioxidant	112

		ROS, NO production; Ames test				
Phyllanthus emblica (Amla)	In vitro enzymatic assays	DPPH, ABTS; MMP & elastase inhibition assays	↑ Antioxidant activity ↓ MMP/elastase activity	Inhibition of collagen and elastin degradation	Skin anti-aging; Antioxidant	113
Phyllanthus emblica (Amla)	In vitro & In silico	RBC membrane stabilization, 15-LOX inhibition; antioxidant assays	Membrane stabilization; blocks 15-LOX mediated inflammation	Epicatechin/catechin-mediated LOX inhibition; radical scavenging	Antioxidant, Anti-inflammatory, anticoagulant	114

Unlike *Tinospora cordifolia* and *Tribulus terrestris* where many individual alkaloids have been tested at length for their anti-aging properties, the majority of tests on *Phyllanthus emblica* are that of whole plant extracts rather than isolated alkaloids. While detailed research in terms of certain alkaloidal constituency is still scarce, existing studies show that *P. emblica* extract has noteworthy antioxidant, anti-inflammatory, chemopreventive and cytoprotective properties most of these processes are connected with aging and age-associated diseases.

Experimental Research collectively, the data demonstrate that *P. emblica* extracts prolong life span in C. elegans and increase stress resistance likely through the modulation of conserved longevity signaling pathways [14]. These effects are mainly due to the rich phytochemical composition of the plant, especially polyphenols and flavonoids like quercetin, myricitin, gallic acid, ellagic acid, catechin and chlorogenic acid. These compounds have powerful antioxidant activity because they can scavenge reactive oxygen species (ROS) and up-regulate endogenous antioxidant enzymes such as superoxide dismutase, catalase, etc., which maintains the redox homeostasis of cells [110-114].

Besides diminishing oxidative stress, *P. emblica* extracts can also enhance thermotolerance and longevity in C. elegans while decreasing the activity of acetylcholinesterase and butyrylcholinesterase with neuroprotective potential. In addition, preclinical trials have shown inhibition of carcinogen-induced preneoplastic lesions from rat livers and colon, and suppression of inflammatory mediators including reactive oxygen species and nitric oxide. The extracts also displayed anti-mutagenic activity in bacterial models against the mutation process, possibly suggesting their role in preserving genomic integrity. These results suggest that P. emblica exerts anti-aging effects via multi-targeted pathways involving reduction of oxidative stress, regulation of inflammation and cellular protection mechanisms. While the role of alkaloids is still only broadly understood, the combined phytochemicals act synergistically to support cell resilience making AMTs important dietary add-ons for longevity-promoting activities[110-114].

The Rasayana Alkaloid Longevity Framework (RALF) in Aging Modulation

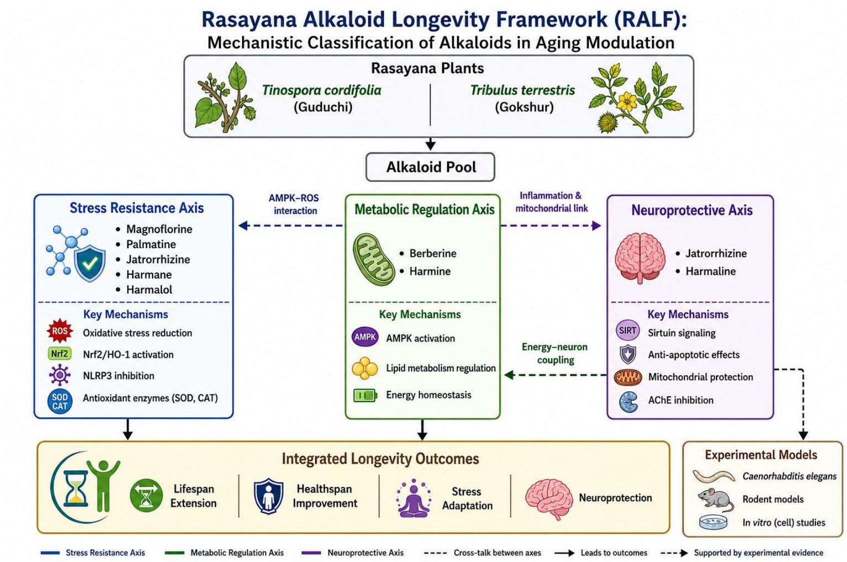

Figure 4. Rasayana Alkaloid Longevity Framework (RALF)

Rasayana Alkaloids which is a framework for longevity categorises alkaloids from *Tinospora cordifolia* and *Tribulus terrestris* on three functional axes, resistance, metabolic regulation and neuroprotection. These compounds activate key pathways associated with aging, including reduction of oxidative stress; activation of AMPK pathway and Sirtuin signalling that leads to improved cellular homeostasis. These pathways are integrated and crosstalk to promote positive effects including improved stress adaptation, metabolic homeostasis and neuroprotection that help drive increased lifespan and healthspan in In vitro, C. elegans and rodent studies.The model (RALF) is designed exclusively around mechanisms of aging modulation mediated by alkaloids and phyllanthus emblica was not included in the model. Unlike much of the other material herein on *Tinospora cordifolia* and on *Tribulus terrestris* (both herbal sources that yield single well-defined alkaloids), any anti-aging effects attributed to *Phyllanthus emblica* appear mostly focused on polyphenols, whole-extract activity, and not alkaloidal constituents specifically.

CONCLUSION

Bioactivity data on alkaloids isolated from the plants *Tinospora cordifolia*, *Tribulus terrestris* and *Phyllanthus emblica* are reviewed in this article, and the published evidence of both in vitro and preclinical activity (antioxidant, anti-inflammatory, antimicrobial/anti-fungal and cytoprotective) is tabulated. From a mechanistic point of view, these compounds can act on some highly conserved longevity pathways, such as insulin/IGF-1 signalling, FOXO activation and AMPK/mTOR regulation as well as autophagyand stress response networks that influence cellular homeostasis and metabolic balance and resilience. Their ability to modulate redox homeostasis, suppress chronic inflammation and preserve proteostasis indicates that they could play a role in blunting age-associated functional decline.

Anyway, the available evidence is mainly preclinical, poorly validated in standardised models of mammalian lifespan and lacks resolution of mechanisms. The non-standardisation of compounds and the variability in extract composition, also hinder translational applicability. Future studies should focus on mechanistic validation in physiologically relevant models, the integration of multi-omics approaches and stringent standardisation of bioactive alkaloids. Data obtained from long-term in vivo studies and biomarker driven clinical investigations are necessary for establishing safety, efficacy and therapeutic relevance. These combined efforts will decide whether Rasayana-originating alkaloids can translate into viable healthy aging therapies.

Disclosure statement

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REFERENCES

1. Chen X, Bahramimehr F, Shahhamzehei N, Fu H, Lin S, Wang H, et al. Anti-aging effects of medicinal plants and their rapid screening using the nematode Caenorhabditis elegans. Phytomedicine. 2024;155665. doi:10.1016/j.phymed.2024.155665.
2. Holliday R. Chance and longevity. Bioessays.

1995;17(5):465–7.
3. da Costa JP, Vitorino R, Silva GM, Vogel C, Duarte AC, Rocha Santos T. A synopsis on aging—theories, mechanisms and future prospects. Ageing Res Rev. 2016;29:90–112.
4. David DC. Aging and the aggregating proteome. Front Genet. 2012;3:247.
5. Lindner AB, Demarez A. Protein aggregation as a paradigm of aging. Biochim Biophys Acta. 2009;1790(10):980–96.
6. Ye Y, Gu Q, Sun X. Potential of Caenorhabditis elegans as an antiaging evaluation model for dietary phytochemicals: a review. Compr Rev Food Sci Food Saf. 2020;19(6):3084–105.
7. Tatiya U, Shastri KV, Surana SJ. Preparation and standardization of polyherbal Rasayana by fermentation process. Pharmacogn Mag. 2008;4(Suppl 15):S100.
8. Vagbhata AH. Rasayana adhyaya. In: Sthana U, editor. Hindi commentary by Kashinath Shastri. Varanasi: Krishnadas Academy; 1994:637.
9. Sharma PV. Dravyaguna Vijnana. Vol. II. Varanasi: Chaukhamba Bharati Academy; 2006.
10. Baliga MS, Dsouza JJ. A review on the chemistry and pharmacology of Phyllanthus emblica. Indian J Pharm Sci. 2011;73(2):163–70.
11. Saha S, Ghosh S. Tinospora cordifolia: one plant, many roles. Anc Sci Life. 2012;31(4):151–9.
12. Ahuja V, et al. Pharmacological properties of Tribulus terrestris: a review. J Pharm Res. 2014;8(9):1143–50.
13. Nair PKR, et al. Immunomodulatory and antitumor activities of Tinospora cordifolia. Int Immunopharmacol. 2004;4(13):1645–59.
14. Sharma U, Bala M, Kumar N, Singh B, Munshi RK, Bhalerao S. Immunomodulatory active compounds from Tinospora cordifolia. J Ethnopharmacol. 2012;141(3):918–926.
15. Kumar M, Hasan M, Sharma A, Suhag R, et al. Tinospora cordifolia (Willd.) Hook.f. & Thomson polysaccharides: a review on extraction, characterization, and bioactivities. Int J Biol Macromol. 2023;229:463-475.
16. Singh J, Saxena E. Immunomodulatory properties of Tinospora cordifolia. Heliyon. 2024;10(5):e40948.
17. Yates CR, et al. Tinospora cordifolia: a review of its immunomodulatory and pharmacological properties. J Diet Suppl. 2022;19(2):271-285.
18. Panchabhai TS, et al. Validation of therapeutic claims of Tinospora cordifolia. Phytother Res. 2008;22(4):425-427.
19. Chhatre S, Nesari T, Somani G, Kanchan D, Sathaye S. Phytopharmacological overview of Tribulus terrestris. Pharmacogn Rev. 2014;8(15):45–51.
20. Baliga MS, Dsouza JJ. Amla (Phyllanthus emblica) and its pharmacological potential: A review. J Ethnopharmacol. 2011;133(2):247–255.
21. Hopkins AL. Network pharmacology: The next paradigm in drug discovery. Nat Chem Biol. 2008;4(11):682–690.
22. Roy A. A review on the alkaloids: an important therapeutic compound from plants. Int J Plant Biotechnol. 2017;3:1–9.
23. 23Hardie DG. AMP-activated protein kinase, an energy sensor that regulates all aspects of cell function. Genes Dev. 2011;25:1895–1908.
24. Srivastava D, Arya U, Soundararajan T, Dwivedi H, Kumar S, Subramaniam JR. Reserpine can confer stress tolerance and lifespan extension in the nematode Caenorhabditis elegans. Biogerontology. 2008;9:309–16.
25. Li H, Roxo M, Cheng X, Zhang S, Cheng H, Wink M. Pro-oxidant and lifespan extension effects of caffeine and related methylxanthines in Caenorhabditis elegans. Food Chem X. 2019;1:100005.
26. Ding AJ, Zheng SQ, Huang XB, Xing TK, Wu GS, Sun HY, et al. Current perspective in the discovery of anti-aging agents from natural products. Nat Prod Bioprospect. 2017;7:335–404.
27. Singh D, Chaudhuri PK. Chemistry and pharmacology of Tinospora cordifolia. Nat Prod Commun. 2017;12(2):299–308.
28. Tiwari P, Nayak P, Prusty SK, Sahu PK. Phytochemistry and pharmacology of Tinospora cordifolia: a review. Syst Rev Pharm. 2018;9(1):70–8.
29. Upadhyay AK, Kumar K, Kumar A, Mishra HS. Tinospora cordifolia (Guduchi): validation of Ayurvedic pharmacology through experimental and clinical studies. Int J Ayurveda Res. 2010;1(2):112–21.
30. Singh N, Kumari S, Singh A, et al. Phytopharmacological characteristics of Tribulus terrestris. Int J Agric Ext Soc Dev. 2022;5(1):83–7.
31. Semerdjieva IB, Zheljazkov VD. Chemical constituents, biological properties, and uses of Tribulus terrestris: a review. Nat Prod Commun. 2019;14(8):1–26.
32. Khan MI, Sri Harsha PSC, Giridhar P, Ravishankar GA. Phytochemical and pharmacological studies on β-carboline alkaloids from Tribulus terrestris. J Ethnopharmacol. 2021;267:113490.
33. Tiwari P, Nayak P, Prusty SK, Sahu PK. Phytochemistry and pharmacology of Emblica officinalis: a review. Syst Rev Pharm. 2019;10(1):10–20.
34. Sharma P, Dwivedee BP, Bisht D, Dash AK, Kumar D. Phytochemical and pharmacological profile of Emblica officinalis (Amla). Heliyon. 2019;5(9):e02437.
35. Labunskyy VM, Gladyshev VN. Role of reactive oxygen species-mediated signaling in aging. Antioxid Redox Signal. 2013;19(12):1362–1372.
36. Chistyakova OV. Signaling pathway of insulin and insulin-like growth factor 1 (IGF-1) as a potential regulator of lifespan. J Evol Biochem Physiol. 2008;44(1):1–11.

37. Mathew R, Pal Bhadra M, Bhadra U. Insulin/insulin-like growth factor-1 signalling (IIS) based regulation of lifespan across species. Biogerontology. 2017;18:35–53.
38. Martins R, Lithgow GJ, Link W. Long live FOXO: unraveling the role of FOXO proteins in aging and longevity. Cell Biosci. 2016;6:45.
39. Eijkelenboom A, Burgering BM. FOXOs: signalling integrators for homeostasis maintenance. Nat Rev Mol Cell Biol. 2013;14(2):83–97.
40. Webb AE, Brunet A. FOXO transcription factors: key regulators of cellular quality control. Trends Biochem Sci. 2014;39(4):159–169.
41. Willcox BJ, Donlon TA, He Q, Chen R, Grove JS, Yano K, et al. FOXO3A genotype is strongly associated with human longevity. Proc Natl Acad Sci U S A. 2008;105(37):13987–13992.
42. Bjedov I, Rallis C. The target of rapamycin signalling pathway in ageing and lifespan regulation. Genes. 2020;11(9):1043.
43. Madeo F, Zimmermann A, Maiuri MC, Kroemer G. Essential role for autophagy in life span extension. J Clin Invest. 2015;125(1):85–93.
44. Johnson SC, Rabinovitch PS, Kaeberlein M. mTOR is a key modulator of ageing and age-related disease. Nature. 2013;493:338–345.
45. Shore DE, Carr CE, Ruvkun G. Induction of cytoprotective pathways is central to the extension of lifespan conferred by multiple longevity pathways. PLoS Genet. 2012;8(7):e1002792.
46. Tabibzadeh S. Signaling pathways and effectors of aging. Front Biosci (Landmark Ed). 2021;26:50–96.
47. Bhandari C. Vanaushadhi Chandrodaya. Vol. 3. Varanasi: Chaukhamba Sanskrit Sansthan; 2006. p. 86.
48. Patwardhan B, Gautam M. Drug discovery through Ayurveda. Drug Discov Today. 2005;10:495–502.
49. Patil M, Patki P, Kamath HV, Patwardhan B. Indian drugs. Ind Drugs. 1997;34:211–215.
50. Premila MS. Ayurvedic herbs: a clinical guide to the healing plants of traditional Indian medicine. New York: Haworth Press; 2006. p. 69–76, 175–176.
51. Pendse VK, Mahavir MM, Khanna KC, Somani SK. Anti-inflammatory and related activity of Tinospora cordifolia (Neem giloe). Indian Drugs. 1981;19:14–71.
52. Singh J, Sinha K, Sharma A, Mishra NP, Khanuja SP. Traditional uses of Tinospora cordifolia (Guduchi). J Med Aromat Plant Sci. 2003;25:748–751.
53. Mia MMK, Kadir MF, Hossan MS, Rahmatullah M. Medicinal plants of the Garo tribe inhabiting the Madhupur forest region of Bangladesh. Ethnobot Res Appl. 2009;7:203–218.
54. Jain S, Sherlekar B, Barik R. Evaluation of antioxidant potential of Tinospora cordifolia and Tinospora sinensis. Int J Pharm Sci Res. 2010;1(11):122–128.
55. Chintalwar G, Jain A, Sipahimalani A, Banerji A, Sumariwalla P, Ramakrishnan R, et al. Phytochemistry. 1999;52:1089–1093.
56. Bisset N, Nwaiwu J. Planta Med. 1983;48:275–279.
57. Khosa RL, Prasad S. Pharmacognostical studies on Guduchi (Tinospora cordifolia Miers). J Res Ind Med. 1971;6:261–269.
58. Upadhyay AK, Kumar K, Kumar A, Mishra HS. Tinospora cordifolia (Willd.) Hook f. and Thoms (Guduchi): validation of Ayurvedic pharmacology through experimental and clinical studies. Int J Ayurveda Res. 2010;1(2):112.
59. Rout GR. Identification of Tinospora cordifolia (Willd.) Miers ex Hook f. Thoms using RAPD markers. Z Naturforsch C. 2006;61(1–2):118–122.
60. Patel SS, Shah RS, Goyal RK. Antihyperglycemic, antihyperlipidemic and antioxidant effects of Dihar, a polyherbal Ayurvedic formulation in streptozotocin-induced diabetic rats. Indian J Exp Biol. 2009;47:564–570.
61. Gupta R, Sharma V. Ameliorative effects of Tinospora cordifolia root extract on histopathological and biochemical changes induced by aflatoxin-B1 in mice kidney. Toxicol Int. 2011;18(2):94.
62. Jagetia GC, Rao SK. Evaluation of the antineoplastic activity of Guduchi (Tinospora cordifolia) in Ehrlich ascites carcinoma-bearing mice. Biol Pharm Bull. 2006;29(3):460–466.
63. Devprakash SK, Subburaju T, Gurav S, Singh S. Tinospora cordifolia: a review on its ethnobotany, phytochemical and pharmacological profile. Asian J Biomed Pharm Sci. 2011;4(1):291–302.
64. Durmaz L, Kiziltas H, Guven L, Karagecili H, Alwasel S, Gulcin I. Antioxidant, antidiabetic, anticholinergic, and antiglaucoma effects of magnoflorine. Molecules. 2022;27(18):5902.
65. Wang L, Yang Y, Sun H, Fei M. Magnoflorine alleviates nonalcoholic fatty liver disease by modulating lipid metabolism, mitophagy and inflammation. Prostaglandins Other Lipid Mediat. 2025;106997.
66. Chow YL, Sato F. Screening of isoquinoline alkaloids for potent lipid metabolism modulation with Caenorhabditis elegans. Biosci Biotechnol Biochem. 2013;77(12):2405–2412.
67. Xu Z, Feng W, Shen Q, Yu N, Yu K, Wang S, et al. Rhizoma coptidis and berberine as a natural drug to combat aging and aging-related diseases via anti-oxidation and AMPK activation. Aging Dis. 2017;8(6):760.
68. Jia W, Su Q, Cheng Q, Peng Q, Qiao A, Luo X, et al. Neuroprotective effects of palmatine via enhancement of antioxidant defense and small heat shock protein expression in Aβ-transgenic Caenorhabditis elegans. Oxid Med Cell Longev. 2021;2021:9966223.
69. Mridula S, Masroor WS, Xavier M, Hui TW, Chan HK, Chirara K, et al. Antioxidant and anti-advanced glycation end products formation properties of palmatine. J Pharm Pharmacogn Res. 2021;9:366–378.

70. Luo T, Zhang H, Zhang WW, Huang JT, Song EL, Chen SG, et al. Neuroprotective effect of jatrorrhizine on hydrogen peroxide-induced cell injury and its potential mechanisms in PC12 cells. Neurosci Lett. 2011;498(3):227–231.
71. Taechowisan T. Antibacterial and cytotoxicity activities of major compounds from Tinospora cordifolia Willd. growing on Mangifera indica L. Int J Nutr. 2019. doi:10.14302/issn.2379-7835.ijn-19-2690.Liu SJ, Yang C, Zhang Y, Su RY, Chen JL, Jiao MM, et al. Neuroprotective effect of β-asarone against Alzheimer's disease: regulation of synaptic plasticity by increased expression of SYP and GluR1. Drug Des Devel Ther. 2016;10:1461–1469.
72. Pokrywka A, Obminski Z, Malczewska-Lenczowska J, Fijalek Z, Turek-Lepa E, Grucza R. Insights into supplements with Tribulus terrestris used by athletes. J Hum Kinet. 2014;41:99–105.
73. Trease GE, Evans WC. A taxonomic approach to the study of medicinal plants and animal derived drugs. In: Trease and Evans Pharmacognosy. 15th ed. Singapore: Harcourt Brace and Company Asia Pvt Ltd; 2002. p. 27.
74. Scott JK. Variation in populations of Tribulus terrestris (Zygophyllaceae). I. Burr morphology. Aust J Bot. 1996;44(2):175–190.
75. Kevalia J, Patel B. Identification of fruits of Tribulus terrestris Linn. and Pedalium murex Linn.: a pharmacognostical approach. Ayu. 2011;32(4):550–553.
76. Adaikan PG, Gauthaman K, Prasad NV. History of herbal medicines with insight into pharmacological properties of Tribulus terrestris. Aging Male. 2001;4(3):163–169.
77. Budantsev AL. Plant resources of Russia: wild flowering plants, their component composition and biological activity. Vol. 3. St. Petersburg: KMK Scientific Press; 2010. p. 102–105.
78. Dinchev D, Janda B, Evstatieva L, Oleszek W, Aslani MR, Kostova I. Distribution of steroidal saponins in Tribulus terrestris from different geographical regions. Phytochemistry. 2008;69(1):176–186.
79. Shishovska M, Arsova-Sarafinovska Z, Memeti S. A simple method for determination of protodioscin in Tribulus terrestris and pharmaceuticals by HPLC-DAD. J Chem Eng Res Updates. 2015;2:12–21.
80. Khudenko PE, Tereshina NS, Morokhina SL. Determination of flavonoids in Tribulus terrestris by HPLC. Pharmacy. 2016;65(5):19–22.
81. Ashwani K. Comparative and quantitative determination of quercetin and other flavonoids in North Indian population of Tribulus terrestris by HPLC. Int J Pharma Bio Sci. 2012;3(4):69–79.
82. Noori M, Dehshiri MM, Zolfaghari MR. Tribulus terrestris (Zygophyllaceae) flavonoid compounds. Int J Mod Bot. 2012;2:35–39.
83. Umarova GK. Lipids of Tribulus terrestris growing in Uzbekistan. Pharmacy. 2015;6:19–21.
84. Samy MN, Bishr MM, Ahmed AA, Sayed HM, Kamel MS. Pharmacognostical studies on flower of Tribulus terrestris. J Pharmacogn Phytochem. 2013;1(5):18–22.
85. Zhu W, Du Y, Meng H, Dong Y, Li L. A review of traditional pharmacological uses, phytochemistry, and pharmacological activities of Tribulus terrestris. Chem Cent J. 2017;11(1):1–16.
86. Azam F, Munier S, Batool M, Ahmad B, Abbas G. Advancements in ethnomedicine and phytochemistry of Tribulus terrestris. Int J Biosci. 2019;14(1):21–37.
87. Tosun F, Tanker M, Tosun A. Alkaloids of Tribulus terrestris L. growing in Turkey. Fabad J Pharm Sci. 1994;19:149–151.
88. Jakobsen H, Bojer MS, Marinus MG, Xu T, Struve C, Krogfelt KA, et al. The alkaloid compound harmane increases the lifespan of Caenorhabditis elegans during bacterial infection by modulating innate immune response. PLoS One. 2013;8(3):e60519.
89. Di Giorgio C, Delmas F, Ollivier E, Elias R, Balansard G, Timon-David P. In vitro activity of β-carboline alkaloids harmane, harmine and harmaline against Leishmania infantum. Exp Parasitol. 2004;106(3–4):67–74.
90. Tse TS, Mak IT, Dickens BF. Antioxidative properties of harmane and β-carboline alkaloids. Biochem Pharmacol. 1991;42(3):459–464.
91. Farzin D, Mansouri N. Antidepressant-like effect of harmane and other β-carbolines in mouse forced swim test. Eur Neuropsychopharmacol. 2006;16(5):324–328.
92. Ghanbari A, Jalili C, Shahveisi K, Akhshi N. Harmine exhibits anti-apoptotic properties and reduces diabetes-induced testicular damage in rats. Clin Exp Reprod Med. 2024;51(4):324.
93. Alzahrani S, Ezzat W, Elshaer RE, Abd El-Lateef AS, Mohammad HMF, Elkazaz AY, et al. Standardized Tribulus terrestris extract protects against rotenone-induced oxidative damage and dopaminergic neuronal loss in mice. J Physiol Pharmacol. 2018;69(6):979–994.
94. Timbilla AA, Vrabec R, Havelek R, Rezacova M, Chlebek J, Blunden G, et al. Anticancer properties of harmine and its derivatives. Phytochem Rev. 2025;24(2):1535–1564.
95. Ahmad A, Khan KA, Sultana S, Siddiqui BS, Begum S, Faizi S, et al. In vitro antimicrobial activity of harmine, harmaline and their derivatives. J Ethnopharmacol. 1992;35(3):289–294.
96. Hilber P, Chapillon P. Effects of harmaline on anxiety-related behavior in mice. Physiol Behav. 2005;86(1–2):164–167.
97. Shariat Razavi SA, Taghdisi Khaboushan M, Jafari R, Shahini A, Ferns GA, Bahrami A. Harmaline induces apoptosis and inhibits migration in A2780 ovarian cancer cells in vitro. Physiol Rep. 2024;12(6):e15984.
98. El Gendy MA, Soshilov AA, Denison MS, El-Kadi AO. Harmaline and harmalol inhibit CYP1A1 via

transcriptional and posttranslational mechanisms. Food Chem Toxicol. 2012;50(2):353–362.
99. Lee CS, Han ES, Jang YY, Han JH, Ha HW, Kim DE. Protective effect of harmalol and harmaline on MPTP neurotoxicity and mitochondrial damage. J Neurochem. 2000;75(2):521–531.
100. Aarons DH, Rossi GV, Orzechowski RF. Cardiovascular actions of harmine, harmaline and harmalol. J Pharm Sci. 1977;66(9):1244–1248.
101. Khan H. Role of Emblica officinalis in medicine. Bot Res Int. 2009;2(4):218-228. Available from: http://www.idosi.org/bri/2(4)09/1.pdf
102. Kirtikar KR, Basu BD. Terminalia chebula. In: Indian medicinal plants. Vol. 1. 1935. p. 1020-3.
103. Unander DW, Webster GL, Blumberg BS. Usage and bioassays in Phyllanthus (Euphorbiaceae). IV. Clustering of antiviral uses and other effects. J Ethnopharmacol. 1995;45:1-18.
104. Indian medicinal plants: a compendium of 500 species. Part 3. Orient Longman Publications; 1997. p. 256-63.
105. Habibur R, Yasin KA, Choudhary MA, Khaliq N, Attaur R, Choudhary MI, et al. Studies on the chemical constituents of Phyllanthus emblica. Nat Prod Res. 2007;21:775-81.
106. Bhattacharya A, Chatterjee A, Ghosal S, Bhattacharya SK. Antioxidant activity of active tannoid principles of Emblica officinalis (amla). Indian J Exp Biol. 1999;37:676-80.
107. Naik GH, Priyadarsini KI, Bhagirathi RG, Mishra B, Mishra KP, Banavalikar MM, et al. In vitro antioxidant studies and free radical reactions of triphala and its constituents. Phytother Res. 2005;19:582-6.
108. Zhang LZ, Zhao WH, Guo YJ, Tu GZ, Lin S, Xin LG. Studies on chemical constituents in fruits of Tibetan medicine Phyllanthus emblica. China J Chin Mater Med. 2003;28:940-3.
109. Zhang YJ, Nagao T, Tanaka T, Yang CR, Okabe H, Kouno I. Antiproliferative activity of the main constituents from Phyllanthus emblica. Biol Pharm Bull. 2004;27:251-5.
110. Wu M, Cai J, Fang Z, Li S, Huang Z, Tang Z, et al. The composition and anti-aging activities of polyphenol extract from Phyllanthus emblica L. fruit. Nutrients. 2022;14(4):857.
111. Pathak P, Prasad BG, Murthy NA, Hegde SN. Effect of Emblica officinalis diet on lifespan, sexual behavior and fitness characters in Drosophila melanogaster. AYU. 2011;32(2):279–284.
112. Kumar G, Madka V, Pathuri G, Ganta V, Rao CV. Molecular mechanisms of cancer prevention by gooseberry (Phyllanthus emblica). Nutr Cancer. 2022;74(7):2291–2302.
113. Pientaweeratch S, Panapisal V, Tansirikongkol A. Antioxidant, anti-collagenase and anti-elastase activities of Phyllanthus emblica, Manilkara zapota and silymarin: an in vitro comparative study for anti-aging applications. Pharm Biol. 2016;54(9):1865–1872.
114. Sharif MA, Khan AM, Salekeen R, Rahman MH, Mahmud S, Bibi S, et al. Phyllanthus emblica methanolic extract regulates multiple checkpoints in 15-lipoxygenase-mediated inflammopathies: computational simulation and in vitro evidence. Saudi Pharm J. 2023;31(8):101681.