

REVIEW ARTICLE

Therapeutic Evaluation of Unani Medicine, Including Single Drugs and Polyherbal Formulations with Special Reference to Neurodegenerative Disorders

Saba Imran, MD; Wasim Ahmad, MD; Sabba Saltanat

ABSTRACT

Ethnopharmacological relevance • Unani remedies are considered safe and can be utilized as a healthcare resource due to the adverse effects of conventional pharmaceuticals. For instance, Donepezil, used to treat alzheimer's disease exerts many adverse effects such as dizziness, vertigo, dryness of mouth. Similarly, Memantine used to slow the neurotoxicity involved in alzheimer's disease also exerts adverse effects like vomiting, tremors and sleep disturbance. Over sixty percent of drugs are derived from synthetic basis, highlighting the potential benefits of natural Unani treatments as a safer alternative.

Neurodegenerative disorders are illnesses characterized by structural and functional deterioration due to abnormal protein aggregation, resulting in inflammation and oxidative stress in the central nervous system. In unani system of medicine all current brain ailments, including alzheimer's disease, parkinson's disease, mania, anxiety, melancholia and others are classified under the general category of neurodegenerative disorders. Their pathogenic variables and associated symptoms and therapeutic modalities are similar. This study focuses on evidence-based Unani herbs and polyherbal formulations for the treatment of various neurodegenerative disorders. It reveals that 43 ethnomedicinal plants can be employed to treat the symptoms of neurodegenerative disorders. The material was gathered from several sources that tabulated the specific details of individual herbs and polyherbal formulations and highlighted the importance of various phytoconstituents on neuroprotective action. The research provides in vivo and scientific evidence to support the use of ethnomedicine in treating neurodegenerative disorders.

Aim of the study • This study aims to validate the efficacy of Unani medicines, traditionally used for neurodegenerative disorders through evidence-based research

Methods • To scan single and polyherbal formulations for neurodegenerative disorders, a literature review of traditional Unani medicine texts was conducted. To collect evidence on the efficacy of these indicated medications in the treatment of neurodegenerative disorders, electronic resources such as ScienceDirect, PubMed, Wiley Online Library, and Google Scholar were searched. The current study is

a systematic review that applies inclusion and exclusion criteria rooted in the classical symptoms of neurological disorders. It evaluates the efficacy of individual herbs and polyherbal formulations recommended by Unani scholars for treatment perspectives.

Results • The researchers have so far discovered 43 single drugs and 38 polyherbal formulations in Unani classical literature for treating various neurodegenerative disorders. These herbs have antioxidant, anti-Alzheimer's, anti-Parkinsonism, anti-convulsant, cognitive enhancer, anti-anxiety, neuroprotective, and anti-depressant properties, with clinical investigations proving their efficacy. The study exclusively focuses on systematic review, highlighting selected clinical studies to assess their quality and reliability of evidence. These are discussed in the introduction to provide context and understanding.

Conclusions • After a thorough review of entire literature of Unani medicine, it is evident that has painstakingly focused more on physiopathology of diseases of *Dimāgh wa Asāb* including their treatment protocols. These protocols include *Istifrāgh* (biopurification), *Taskhīn* (producing warmth), *Tajfīf* (desiccation), *Tafrih-i Taba'* (exhilaration). Research into Unani medicine has shown promising results, particularly in the use of medicinal plants known for their neuroprotective properties. One of the key advantages of Unani herbs is their natural composition, which typically consists of bioactive compounds that exert neuroprotective effects without the harsh impact often associated with synthetic drugs. For instance, herbs like Brahmi (*Bacopa monnieri*), Waj Turki (*Acorus calamus*), Chilghoza (*Pinus gerardiana* Wall) and Asgand (*Withania somnifera*) and many other plants have been studied for their ability to enhance cognitive function, reduce oxidative stress, and support neuronal health. These herbs work through various mechanisms such as antioxidant activity, anti-inflammatory properties, and modulation of neurotransmitter levels, all of which contribute to their neuroprotective potential. Nevertheless some of the compound formulations presented, that, have not yet undergone clinical testing. As a result, the researchers are advised to validate those medicines that have not yet undergone clinical evaluation. (*Altern Ther Health Med*. 2024;30(9):54-64).

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INTRODUCTION

Neurologic conditions are widespread and extensive and affects millions of people worldwide. Alzheimer's disease (AD), parkinson's disease (PD) and ischemia/stroke are most common of them. As per the data from the Alzheimer's Diseases Association as many as 6.7 million people have Alzheimer's disease in United States whereas according to Parkinson's Diseases Foundation almost a million American living with this disease. A study was published by Lancet *Neurology* in 2021 that shows more than 3 billion people

living with a neurological disorders. 7.4% among adults over the age of 60 in India are currently living with alzheimers dementia.¹ These figures are only anticipated to rise in tandem with the aging of the global population. Neurodegenerative diseases arise from the gradual loss of nerve cells in the brain or peripheral nervous systems which ultimately leads to their death.^{2,3} Neurodegenerative disorders (NDDs) are a broad category of diseases characterized by progressive structural and functional degradation due to the accumulation of abnormal protein aggregation that leads to inflammation as well as oxidative stress in the CNS.⁴ Numerous biological mechanisms, including abnormal ubiquitination, mitochondrial dysfunction, excitotoxicity of neurons, disruption of the blood-brain barrier, oxidative stress, protein aggregates in neurons, depletion or insufficient synthesis of neurotransmitters, degradation of neurotransmitters in the synaptic cleft due to higher enzyme activity have been linked to neurodegenerative disorders.^{5,6} The correct approach starts with the patient to concentrate on the clinical issues in terms of anatomy and pathophysiology first. Only then can a specific neurologic diagnosis be considered. White matter, sensory visual, and cerebellar pathways are affected while primary neuronal abnormalities or seizures occur.

Currently, therapies for neurodegenerative illnesses focus on delaying the disease progression, enhancing the patient's quality of life, and managing co-morbid disorders.⁷ In the Unani system of medicine, neurodegenerative disorders are classified based on temperamental pathology, which involves an imbalance of the qualities (*Kaifiyyāt*) such as hotness, coldness, moistness, and dryness, as well as compound qualities like hot-dry, hot-moist, cold-dry, and cold-moist. Any alteration in the temperament/*Mizaḥ* (referred to as dystemperament or *Su⁷-i Mizaḥ*, whether it is *Sāda*(merely change in qualities) or *Māddī*(abnormal substantial temperament), disrupts the organ's function and can lead to the manifestation of disease. Ibn Zuhr in his book *Kitabut Taiseer*, mentioned that *Su⁷-i Mizaḥ* particularly *Su⁷-i Mizaḥ Yābis*, leads to the destruction of the *Jawhar*(essence) of the brain and nerves which leads to degenerative disorders.^{8,9} Neurodegenerative disorders are often linked to imbalances or disturbances in these qualities, particularly in the brain. The classification includes:

Amrade Dimāgh (Brain Disorders)

- *R'sha* (Tremors)
- *Tashannuj* (Convulsions/Spasms)
- *Sar'*(Epilepsy)
- *Fālij* (Paralysis)

Amrāde 'Asbi (Nerve Disorders)

- *Laqwa'* (Facial Paralysis)
- *Khābt-e-Dimāgh* (Mental Confusion)

Amrāde Nafsānī (Psychiatric Disorders)

- *Junūn* (Psychosis/Insanity)
- *Zof-e-'Aql* (Weak memory)
- *Malankhūliya* (Melancholia)

Unani scholars have mentioned their etiology, pathophysiology, and principles of treatment.^{10,11} For their treatment, a variety of single herbs^{12,13} and polyherbal formulations¹³⁻¹⁷ in the form of *itrifal*, *khamīra*, *ma'jūn*, and *habb* (pills) have been recommended. Numerous *in-vivo* and *in-vitro* studies have reported the antioxidant, anti-Alzheimer's, anti-Parkinsonism, anti-epileptic, anti-depressive, memory-enhancing, and anti-anxiety characteristics of these drugs. In conventional medicine cell or molecule treated as unit and focal point for treatment because it believes on reductionism approach, whereas, in contrast Unani medicine emphasizes holism, viewing the entire body as a cohesive unit for treatment. Conventional medicine often derives active drug ingredients synthetically, which can lead to harsh effects on the body due to the absence of protective molecules that mitigate antagonistic effects. In contrast, Unani medicine uses whole herbs for treatment, resulting in safer and potentially more effective outcomes compared to conventional approaches. Furthermore, Unani medicine has the unique ability to potentiate organs by maintaining their *Kaifiyyāt* (conditions or Qualities), a concept not typically found in conventional medicine.

Additionally, Unani medicine incorporates the principle of *Tabi'at* (medicatrix naturae/supreme planner), which ensures the internal environment of the body stays within physiological limits, another unique aspect not found in conventional medicine.

On behalf of above properties Unani medicine shows promising results, particularly in the use of medicinal plants known for their neuroprotective properties. One of the key advantages of Unani herbs is their natural composition, which typically consists of bioactive compounds that exert neuroprotective effects without the harsh impact often associated with synthetic drugs. For instance, herbs like Brahmi(Bacopa monnieri), Waj Turki, Chilghoza and Asgand (Withania somnifera) and many other plants have been studied for their ability to enhance cognitive function, reduce oxidative stress, and support neuronal health. These herbs work through various mechanisms such as antioxidant activity, anti-inflammatory properties, and modulation of neurotransmitter levels, all of which contribute to their neuroprotective potential. In this paper, we have undertaken a comprehensive analysis to explore Unani medications that show promising therapeutic efficacy for various NDDs, supported by a wealth of data.

METHODOLOGY

To scan the single herbs and compound formulations recommended in Unani Medicine for the treatment of neurodegenerative disorders, a manual literature survey of classical Unani texts such as *Kamiluṣ Sana'a*, *Alqanoon Fit Tib*, *Zakhira Khwarazm Shahi*, *Kitab Al-Adwiyya wal Aghziyya*, *Kitab al-Mukhtarāt Fit tib*, *Muheet-e-Azam*, *Bayaz-e-Kabeer*, *Qarabadeen Qadri*, *Makhzanul mufradat*, *Khazain-ul Advia* etc., was conducted. Using a book that provides the

Table 1. Brief description of Single herbs recommended for Neurodegenerative disorders

Unani name	Scientific name	Family	Part used	Action in Unani	Therapeutic use in Unani	Dose	Dosage form	Important Formulations	Reference
Āmla	<i>Phyllanthus emblica</i> L.	Phyllanthaceae	Fresh and dried fruits, seeds, nuts, flowers, leaves and bark	<i>Muqawwi-i-Dimagh</i> (Brain tonic), <i>Muqawwi-i-afīza</i> (Memory enhancer)	<i>u'f-i-Dimāgh</i> (Cerebrasthenia)	3-5g	<i>Jawarish</i>	<i>Anoshdārū</i> , <i>Murabbā Āmla</i> , <i>Jawāriṣh-i-Āmla Sāda</i>	91,98
Anjeer	<i>Ficus carica</i> L.	Moraceae	Fruit	<i>Muqawwi-i-arārat Ghariziyya</i> (Tonic for innate heat), <i>Mughadhūdhī</i> (Nutritive)	<i>u'f-i-arārat Ghariziyya</i> (innate heat insufficiency), <i>u'f-i-Ām</i> (General debility)	10-12 nos.	<i>Safīf</i>	<i>Safīf-i-Bara</i>	91,98
Āqar qarha	<i>Anacyclus pyrethrum</i> (L.) Lag.	Asteraceae	Root	<i>Muqawwi-i-Ām</i> (General tonic), <i>Mukhrij-i-Balgham</i> (Expellant of phlegm)	<i>u'f-i-Ām</i> (General debility), <i>Amrā-i-Bārīda Balghamiyya</i> (Cold phlegmatic diseases)	2-3g	<i>Jawāriṣh</i>	<i>Jawāriṣh-i-Zar'ūni</i> , <i>Falāniyya Rūmi</i> , <i>Barshāsha</i>	91,98
Asaroon	<i>Asarum europaeum</i> L.	Aristolochiaceae	Rhizome	<i>Muharrik-i-Asab</i> (nervine stimulant),	<i>Sar'</i> (epilepsy), <i>Falij</i> (paralysis), <i>Istirkh'a</i> (flaccidity), <i>Khadr</i> (numbness), <i>Ra'sha</i> (Tremor), <i>Nisyān</i> (Dementia)	3g	<i>Jawāriṣh</i>	<i>Jawāriṣh-i-Jalīnūs</i>	12,91,98
Asgand	<i>Withania Somnifera</i> (L.) Dunal.	Solanaceae	Dried roots	<i>Muqawwi-i-Ām</i> (General tonic), <i>Muqawwi-i-Āab</i> (Nervine tonic), <i>Munaqi-'r-aṣab</i> (nerve cleanser)	<i>u'f-i-Ām</i> (General debility), <i>u'f-i-Āab</i> (Nervine weakness), <i>Nisyān</i> (Dementia)	5-10g	<i>Habb</i> , <i>Ma'jun</i>	<i>Habb-i-Asgand</i> , <i>Safīf-i-Asgand</i> , <i>Ma'jun</i> , <i>Muqawwi Raim</i>	12,98
Azārāqī	<i>Strychnos nux-vomica</i> L.	Loganiaceae	Seed	<i>Muqawwi-i-Āab</i> (Nervine tonic), <i>Muarrik-i-Āab</i> (Nervine stimulant), <i>Dāfī-i-Amrā Ābāniya</i> (Useful in nervine diseases)	<i>u'f-i-Āab</i> (Nervine weakness)	60-250mg	<i>Habb</i> , <i>Ma'jun</i>	<i>Habb-i-Azārāqī</i> , <i>Ma'jun Azārāqī</i> , <i>Ma'jun Lanā</i>	12,98
Bādām shīrī	<i>Prunus amygdalus</i> Batsch. var. dulces.	Rosaceae	Seed	<i>Muqawwi-i-Dimagh</i> (Brain tonic), <i>Muqawwi-i-Āab</i> (Nervine tonic)	<i>u'f-i-Dimāgh</i> (Cerebrasthenia), <i>u'f-i-Āab</i> (Nervine weakness)	7-11 Seeds	<i>Rawghan</i> , <i>Lubūb</i>	<i>Rawghan Bādām Shīrīn</i> , <i>Lubūb Kabīr</i> , <i>Lubūb aghīr</i>	11,12,98
Bādranjboya	<i>Nepeta hindostana</i> (Roth.) Haines	Lamiaceae	Leaf	<i>Muqawwi-i-arārat Ghariziyya</i> (Tonic for innate heat)	<i>u'f-i-arārat Ghariziyya</i> (innate heat insufficiency)	5-7g	<i>Ma'jun</i>	<i>Ma'jun-i-Khadar</i>	12,98
Balela	<i>Terminalia bellirica</i> Roxb.	Combretaceae	Fruit	<i>Muqawwi-i-Dimāgh</i> (Brain tonic)	<i>u'f-i-Dimāgh</i> (Cerebrasthenia)	5-7g	<i>Itrifal</i>	<i>Itrifal Ustūkhuddūs</i> , <i>Itrifal aghīr</i> , <i>Itrifal Muqil</i>	11,98
Bazr-ul-Banj	<i>Hyoscyamus niger</i> L.	Solanaceae	Seed	<i>Dāfī-i-Tashannuj</i> (Antispasmodic), <i>Mukhaddir</i> (Anaesthetic), <i>Munawwim</i> (Hypnotic), <i>Musakkīn</i> (Sedative)	<i>Amrā Ābāniya</i> (Nervine diseases), <i>Dard wa Alam</i> (Pain), <i>Sahar</i> (Insomnia), <i>Junūn</i> (Mania)	0.5-1g	<i>Lā'ūq</i>	<i>Barshāsha</i> , <i>Lā'ūq Bazr-ul-Banj</i> , <i>Banādīqul Buzūr</i>	11,12
Bisbāsa	<i>Myristica fragrans</i> Hoult.	Myristicaceae	Aril	<i>Muqawwi-i-Dimāgh</i> (Brain tonic)	<i>u'f-i-Dimāgh</i> (Cerebrasthenia)	2-5g	<i>Itrifal</i> , <i>Jawāriṣh</i>	<i>Anoshdārū</i> , <i>Itrifal Kabīr</i> , <i>Jawāriṣh Bisbāsa</i>	11,12,98
Brahmi	<i>Bacopa monnieri</i> (Linn.) Pennel.	Scrophulariaceae	Whole plant	<i>Muqawwi-i-Dimāgh</i> (Brain tonic), <i>Muqawwi-i-Āab</i> (Nervine tonic)	<i>u'f-i-Dimāgh</i> (Cerebrasthenia), <i>u'f-i-Āab</i> (Nervine weakness)	5g	<i>Ma'jun</i>	<i>Ma'jun Brahmi</i>	11,12
Darchini	<i>Cinnamomum verum</i> J. Presl	Lauraceae	Bark	<i>Muqawwi-i-arārat Ghariziyya</i> (Tonic for innate heat)	<i>u'f-i-arārat Ghariziyya</i> (innate heat insufficiency)	1-2g	<i>Jawāriṣh</i> , <i>Rawghan</i>	<i>Jawāriṣh Jalīnūs</i> , <i>Rawghan Dār Chīni</i> , <i>Jawāriṣh Bisbāsa</i>	11,12,98
Filfil Darāz	<i>Piper longum</i> L.	Piperaceae	Fruit	<i>Muqawwi-i-Ām</i> (General tonic), <i>Muqawwi-i-arārat Ghariziyya</i> (Tonic for innate heat)	<i>u'f-i-Ām</i> (General debility), <i>u'f-i-arārat Ghariziyya</i> (Innate heat insufficiency)	500mg-1g	<i>Jawāriṣh</i> , <i>Ma'jun</i>	<i>Jawāriṣh Jalīnūs</i> , <i>Jawāriṣh Bisbāsa</i> , <i>Ma'jun Falāsīfā</i>	11,12,98
Filfil Siyah	<i>Piper nigrum</i> L.	Piperaceae	Fruit	<i>Muqawwi-i-Āab</i> (Nervine tonic)	<i>u'f-i-Āab</i> (Nervine weakness)	1-2g	<i>Jawāriṣh</i> ,	<i>Jawāriṣh Kamūni</i> , <i>Dawā-ul-Shifā</i> , <i>Jawāriṣh Jalīnūs</i>	12,91,98
Gurmar	<i>Gymnema sylvestre</i> R. Br.	Asclepiadaceae	Leaf & Root	<i>Musakkīn-i-Āab</i> (Nervine sedative), <i>Muqawwi-i-Āab</i> (Nervine tonic)	<i>u'f-i-Āab</i> (Nervine weakness)	5-7g	<i>Qur</i>	<i>Qur Dhayābius Khā</i>	12,91
Halela Zard	<i>Terminalia chebula</i> Retz.	Combretaceae	Fruit	<i>Muqawwi-e-Dimagh</i> (Brain tonic), <i>Muqawwi-i-Hafīza</i> (Memory enhancer)	<i>u'f-i-Dimāgh</i> (Cerebrasthenia), <i>u'f-i-afīza</i> (Poor memory)	3-5g	<i>Itrifal</i>	<i>Itrifal Kīshnīzī</i> , <i>Itrifal Ustūkhuddūs</i> , <i>Itrifal Malayīn</i>	11,12,98
Jadwār	<i>Delphinium denudatum</i> Wall.	Ranunculaceae	Root	<i>Muqawwi-i-Āab</i> (Nervine tonic)	<i>u'f-i-Āab</i> (Nervine weakness), <i>Istirkhā</i> (Atony/flaccidity)	0.5-1g	<i>Habb</i> , <i>Khamira</i>	<i>Habb-i-Jadwār</i> , <i>Khamira Gaozabān Ambari Jadwār</i> 'Ud <i>Salīb Wālā</i>	11,12,98
Jawz	<i>Juglans regia</i> L.	Juglandaceae	Kernels	<i>Muqawwi-i-Āā Ra'isa</i> (Tonic for vital organs), <i>Musakkīn-i-Āab</i> (Nervine sedative)	<i>u'f-i-Dimāgh</i> (Cerebrasthenia), <i>u'f-i-Āab</i> (Nervine weakness), <i>u'f-i-afīza</i> (Poor memory)	10-20g	<i>Lubūb</i>	<i>Lubūb-i-Kabīr</i> , <i>Lubūb-i-aghīr</i>	11,12,98
Jawzbuwa	<i>Myristica fragrans</i> Hoult.	Myristicaceae	Fruit	<i>Muqawwi-i-Āab</i> (Nervine tonic)	<i>u'f-i-Āab</i> (Nervine weakness), <i>Amrā-i-Bārīda</i> (Diseases of cold temperament), <i>Istirkhā</i> (Atony), <i>Khadar</i> (Numbness)	1-2g	<i>Jawāriṣh</i> , <i>Ma'jun</i>	<i>Anoshdārū</i> , <i>Jawāriṣh Ood Shirīn</i> , <i>Ma'jun-i-Chob Chīni</i>	11,12,91
Kababa	<i>Piper cubeba</i> L.f.	Piperaceae	Fruit	<i>Muqawwi-i-arārat Ghariziyya</i> (Tonic for innate heat), <i>Muarrik</i> (Stimulant)	<i>u'f-i-arārat Ghariziyya</i> (Innate heat insufficiency),	1-3g	<i>Ma'jun</i>	<i>Ma'jun-i-Anakī</i> , <i>Labāb-i-Soghīr</i>	11,91,98
Khulanjan	<i>Alpinia galanga</i> L. Willd.	Zingiberaceae	Rhizome	<i>Muqawwi-i-Āab</i> (Nervine tonic), <i>Musakkīn</i> (Sedative)	<i>Amrā-i-Āab</i> (Nervine diseases)	2-3g	<i>Jawāriṣh</i> , <i>Habb</i>	<i>Jawāriṣh Jalīnūs</i> , <i>Habb-i-Āmbar</i>	11,91,98
Kundur	<i>Boswellia serrata</i> Triana & Planch.	Bursaceae	Gum/ Exudate	<i>Muqawwi-i-Dimagh</i> (Brain tonic)	<i>u'f-i-Dimāgh</i> (Cerebrasthenia)	3-4g	<i>Ma'jun</i> , <i>Jawāriṣh</i>	<i>Ma'jun Kundur</i> , <i>Jawāriṣh Kundur</i>	11,12,98
Mastagi	<i>Pistacia lentiscus</i> L.	Anacardiaceae	Resin	<i>Muqawwi-i-arārat Ghariziyya</i> (Tonic for innate heat)	<i>u'f-i-arārat Ghariziyya</i> (Innate heat insufficiency)	1-2g	<i>Jawāriṣh</i>	<i>Jawāriṣh Maagi</i> , <i>Jawāriṣh Jalīnūs</i>	11,12,98
Muqil	<i>Commiphora wightii</i> (Arn.)	Bursaceae	Gum/ Exudate	<i>Muqawwi-i-Āab</i> (Nervine tonic)	<i>u'f-i-Āab</i> (Nervine weakness)	1-15g	<i>Habb</i> , <i>Ma'jun</i>	<i>Habb-i-Muqil</i> , <i>Ma'jun Muqil</i>	11,91,98
Rehan	<i>Ocimum sanctum</i> Linn.	Lamiaceae	Leaf	<i>Munafthī-i-Balgham</i> (Expectorant), <i>Muallīl-i-Waram</i> (Anti-inflammatory)	<i>Tap-i-Balghami</i> (Phlegmatic fever)	5-7g	<i>Khamira</i>	<i>Khamira Ābresham</i> 'Ud <i>Maagiwālā</i>	91,98
Ratab	<i>Phoenix dactylifera</i> L.	Arecaceae	Fruit	<i>Muqawwi-i-Āab</i> (Nervine tonic), <i>Muqawwi-i-Ām</i> (General tonic),	<i>u'f-i-Āab</i> (Nervine weakness), <i>u'f-i-Ām</i> (General debility)	10-15g	<i>Ma'jun</i>	<i>Ma'jun Aarad Khurmā</i> , <i>Ma'jun Supārīpāk</i>	91,98
Qust Shirin	<i>Saussurea lappa</i> CB Clarke.	Asteraceae	Root	<i>Muqawwi-i-Āab</i> (Nervine tonic), <i>Mohallīl-i-waram</i> (Anti-inflammatory)	<i>Falij</i> (paralysis), <i>Ra'sha</i> (Tremor), <i>Laqwa</i> (Bells palsy)	2-3g	<i>Jawāriṣh</i>	<i>Jawāriṣh-i-Jalīnūs</i>	12,91,98
Rumman	<i>Punica granatum</i> L.	Lythraceae	Fruit	<i>Muwallīd-i-Dam</i> (Haemopoietic), <i>Muqawwi-i-arārat Ghariziyya</i> (Tonic for innate heat)	<i>Faqraddam</i> (Anemia), <i>u'f-i-arārat Ghariziyya</i> (Innate heat insufficiency)	5-10g	<i>Jawāriṣh</i> , <i>Sharbat</i>	<i>Jawāriṣh Anāay</i> , <i>Sharbat Anār</i> , <i>Jawāriṣh Puḍīna</i>	91,98
Shoneez	<i>Nigella sativa</i> L.	Ranunculaceae	Seed	<i>Muqawwi-i-Āab</i> (Nervine tonic)	<i>u'f-i-Āab</i> (Nervine weakness)	1-2g	<i>Ma'jun</i>	<i>Ma'jun Kalkālanaj</i> , <i>Ma'jun Fanjnos</i>	11,91
Seer	<i>Allium sativum</i> L.	Liliaceae	Bulb	<i>Muqawwi-i-arārat Ghariziyya</i> (Tonic for innate heat), <i>Qatī' Akhlāt-i-Ghalīza</i> (Breaking agent for viscous humour)	<i>u'f-i-arārat Ghariziyya</i> (Innate heat insufficiency), <i>Amrā-i-Bārīda Balghamiyya</i> (Cold Phlegmatic disorders)	2-3g	<i>Ma'jun</i>	<i>Ma'jun Sir</i> , <i>Ma'jun Sir Alvi Khān</i>	11,91
Sumbul-Ut-Teeb	<i>Nardostachys jatamansi</i> DC.	Caprifoliaceae	Rhizome	<i>Muqawwi-i-Dimāgh</i> (Brain tonic)	<i>u'f-i-Dimāgh</i> (Cerebrasthenia)	3-5g	<i>Jawāriṣh</i>	<i>Jawāriṣh Fanjnos</i> , <i>Barsh'sha</i> , <i>Anoshdārū</i>	91,98
Ustūkhuddūs	<i>Lavandula stoechas</i> L.	Lamiaceae	Leaves, flowers, whole plant	<i>Muqawwi-i-Āab</i> (Nervine tonic), <i>Muqawwi-i-Dimāgh</i> (Brain tonic), <i>Muharrik-i-Asab</i> (nervine stimulant)	<i>u'f-i-Āab</i> (Nervine weakness), <i>u'f-i-Dimāgh</i> (Cerebrasthenia)	7-10g	<i>Itrifal</i>	<i>Itrifal Ustūkhuddūs</i>	12,91,98
Waj turki	<i>Acorus calamus</i> L.	Araceae	Rhizome	<i>Muqawwi-i-Āab</i> (Nervine tonic), <i>Muqawwi-i-Dimāgh</i> (Brain tonic)	<i>u'f-i-Āab</i> (Nervine weakness), <i>u'f-i-Dimāgh</i> (Cerebrasthenia)	1-3g	<i>Ma'jun</i>	<i>Ma'jun Vaj</i>	11,12,91
Zafran	<i>Crocus sativus</i> L.	Iridaceae	Style & Stigma	<i>Muqawwi-i-Dimāgh</i> (Brain tonic)	<i>u'f-i-Dimāgh</i> (Cerebrasthenia), <i>Nisyān</i> (dementia)	25-50 mg	<i>Dawa</i>	<i>Dawa ul Kurkum</i> , <i>Daw aul Misk Mo'tadil Sada</i>	12,91,98
Zaitoon	<i>Olea europaea</i> L.	Oleaceae	Fruit oil & Leaf	<i>Muqawwi-i-Āab</i> (Nervine tonic)	<i>u'f-i-Ām</i> (General debility), <i>Nisyān</i> (Forgetfulness)	50ml	<i>Rawghan</i>	<i>Rawghan Zaitūn</i>	11,91
Zanjabeel	<i>Zingiber officinale</i> Rosc	Zingiberaceae	Rhizome	<i>Muqawwi-i-Āab</i> (Nervine tonic)	<i>u'f-i-Āab</i> (Nervine weakness), <i>Nisyān</i> (Forgetfulness)	1-1.5g	<i>Jawāriṣh</i>	<i>Jawāriṣh Zanjabil</i> , <i>Murabbā Zanjabil</i> , <i>Ma'jun Zanjabil</i>	11,91
Zard Chob	<i>Curcuma longa</i> L.	Zingiberaceae	Rhizome	<i>Musakkīn</i> (Soothing agent), <i>Mufattī-i-Sudad</i> (Deobstruent)	<i>u'f-i-Ām</i> (General debility)	5-7g	<i>Sanūn</i> , <i>Safīf</i>	<i>Sanūn-i-Zard</i> , <i>Safīf-i-Ihāl</i> , <i>Rawghan Aurāq Qawī</i>	11,91,98

scientific names of Unani medicinal plants in line with their morphological description, the traditional names of prescribed herbs were matched with the current scientific names. This manual search was conducted over a period of three months, from January to March 2024.

To find proof of the effectiveness of suggested medications in the treatment of neurodegenerative disorders, electronic databases including *ScienceDirect*, *PubMed*, *Wiley Online Library*, and *Google Scholar* were also searched. The search spanned from January 2024 to March 2024. MeSH (medical subject headings) and other pertinent phrases were employed as the main building blocks for the search strategy for electronic database searches. The search terms were explicitly defined and included “Neurodegenerative disorders, Alzheimer’s disease, Parkinson’s disease, Dementia, Cognitive impairment, Nisyān, Ra’sha, Mālanhūliya, Sehar, Saktā, Antioxidant, Memory enhancer, Anti-Alzheimer’s, Anti-parkinsonism, Anti-convulsant, Anti-anxiety, Cognitive enhancer, Neuroprotective and Anti-depressant.” These terms were looked up in conjunction with each recommended drug and formulation, ensuring a comprehensive and targeted search strategy.

Literature Findings

The findings of the literature review are summarised in Tables 1-4. Single herbs and compound formulations recommended by Unani scholars for the treatment of neurodegenerative disorders are listed in Tables 1 and 2

respectively. Table 3 provides the scientific validation studies carried out on polyherbal formulations for the treatment of various ailments including NDDs. Table 4 summarises the pharmacological activities of the proposed herbs in relation to the treatment of neurodegenerative disorders.

Unani Medications for the treatment of Neurodegenerative disorders

Single Herbs. Unani medications that are commonly used in managing the symptoms of neurodegenerative disorders are formulations rather than single herbs, except for a few medicines. According to a literature survey of Unani texts, *Acorus calamus*, *Allium sativum*, *Alpinia galanga*, *Anacyclus pyrethrum*, *Asarum europaeum*, *Bacopa monnieri*, *Boswellia serrata*, *Cinnamomum verum*, *Commiphora wightii*, *Crocus sativus*, *Curcuma longa*, *Delphinium denudatum*, *Ficus carica*, *Gymnema sylvestre*, *Hyoscyamus niger*, *Juglans regia*, *Lavandula stoechas*, *Myristica fragrans*, *Nardostachys jatamansi*, *Nepeta hindostana*, *Nigella sativa*, *Ocimum tenuiflorum*, *Olea europaea*, *Phoenix dactylifera*, *Phyllanthus emblica*, *Piper cubeba*, *Piper longum*, *Piper nigrum*, *Pistacia lentiscus*, *Prunus amygdala*, *Punica granatum*, *Saussurea lappa*, *Strychnos nux vomica*, *Terminalia bellirica*, *Terminalia chebula*, *Withania somnifera*, and *Zingiber officinale* are found as the commonly included ingredients in those formulations which are recommended in NDDs. A brief description of these herbs, including their Unani and scientific names, family, parts used, action, therapeutic use,

Table 2. Compound formulations in Unani Medicine for Neurodegenerative disorders

Compound Formulation	Main Indication	Actions	Dose	Dosage form	Reference
Dawa-ul-Misk Motadil Sada	<i>Du’f-i Adā’ Ra’īsa</i> (General debility), <i>Malikhūliya</i> (Melancholia)	<i>Muqawwī-i Dimāgh</i> (Brain tonic), <i>Muqawwī-i Aām</i> (General tonic)	5-10gm	Semi-solid preparation	13,17
Habb-e-Azaraqī	<i>Fālij</i> (Hemiplegia), <i>Laqwa</i> (Bell’s palsy), <i>Khadar</i> (Numbness)	<i>Muqawwī-i Asāb</i> (Nervine tonic), <i>Muharrīk-i Asāb</i> (Nervine stimulant)	250-500mg	Pills	13,17
Habb-e-Beesh	<i>Du’f-i-Asāb</i> (Nervine weakness)	<i>Muqawwī-i-Asāb</i> (Nervine tonic)	150gm	Semi-solid preparation	17
Habb-e-Bolas	<i>Du’f-i-Asāb</i> (Nervine weakness), <i>Nisyān</i> (Dementia)	<i>Muqawwī-i- Dimāgh</i> (Brain tonic)	5-10gm	Semi-solid preparation	17
Habb-e-Jadwar	<i>Du’f-i-Asāb</i> (Nervine weakness)	<i>Muharrīk-i- Asāb</i> (Nervine stimulant)	250-500mg	Pills	13,16,17
Habb-e-Jalinoos	<i>Du’f-i-Asāb</i> (Nervine weakness)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	500mg-1gm	Pills	13,16,17
Habb-e-Jawahar	<i>Du’f-i-Adā’ Ra’īsa</i> (General debility), <i>Du’f-i-Asāb</i> (Nervine weakness)	<i>Muqawwī-i-Adā’ Ra’īsa</i> (General tonic)	125-250mg	Pills	13,17
Habb-e-Sara	<i>Sar’</i> (Epilepsy)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	250mg	Semi-solid preparation	17
Itrifal Aftimoon	<i>Malikhūliya</i> (Melancholia)	<i>Muqawwī-i- Dimāgh</i> (Brain tonic)	10gm	Semi-solid preparation	13,17
Itrifal Muqawwi Dimagh	<i>Du’f-i-Dimāgh</i> (Cerebrasthenia)	<i>Muqawwī-i- Dimāgh</i> (Brain tonic)	5-10gm	Semi-solid preparation	13,16,17
Itrifal Sagheer	<i>Du’f-i-Dimāgh</i> (Cerebrasthenia), <i>Nisyān</i> (Dementia)	<i>Muqawwī-i- Dimāgh</i> (Brain tonic)	10-15gm	Semi-solid preparation	13,17
Itrifal Zabeeb	<i>Sar’</i> (Epilepsy)	<i>Mufattih-i- Sudad</i> (Deobstruent)	10-15gm	Semi-solid preparation	13,17
Jawarish Shahanshahi Ambari	<i>Du’f-i-Dimāgh</i> (Cerebrasthenia)	<i>Muqawwī-i- Dimāgh</i> (Brain tonic)	5-10gm	Semi-solid preparation	13,17
Jawarish Shahi	<i>Du’f-i-Dimāgh</i> (Cerebrasthenia)	<i>Muqawwī-i- Dimāgh</i> (Brain tonic)	5-10gm	Semi-solid preparation	13
Jawarish Zarooni sada	<i>Du’f-i-Dimāgh</i> (Cerebrasthenia)	<i>Muqawwī-i- Dimāgh</i> (Brain tonic)	5-10gm	Semi-solid preparation	13
Khamira Abresham Hakim Arshad Wala	<i>Du’f-i Adā’ Ra’īsa</i> (General debility), <i>Du’f-i- Umūmi</i> (General weakness)	<i>Muqawwī-i-Adā’ Ra’īsa</i> (General tonic), <i>Muqawwī-i- Aām</i> (General tonic)	3-6gm	Semi-solid preparation	16,17
Khamira Abresham Sheera Unnab wala	<i>Du’f-i-Dimāgh</i> (Cerebrasthenia), <i>Du’f-i-Basār</i> (Poor eyesight)	<i>Muqawwī-i- Dimāgh</i> (Brain tonic), <i>Muqawwī-i- Basar</i> (Eye tonic)	3-6gm	Semi-solid preparation	16,17
Khamira Gaozaban Ambari Jawahar wala	<i>Du’f-i-Dimāgh</i> (Cerebrasthenia), <i>Malikhūliya</i> (Melancholia), <i>Du’f-i-Asāb</i> (Nervine weakness)	<i>Muqawwī-i- Aām</i> (General tonic)	3-6gm	Semi-solid preparation	16,17
Khamira Gaozaban Sada	<i>Du’f-i-Dimāgh</i> (Cerebrasthenia), <i>Malikhūliya</i> (Melancholia)	<i>Muqawwī-i- Dimāgh</i> (Brain tonic), <i>Muqawwī-i- Aām</i> (General tonic)	5-10gm	Semi-solid preparation	13,16,17
Khamira Marwareed	<i>Du’f-i-Asāb</i> (Nervine weakness), <i>Du’f-i-Dimāgh</i> (Cerebrasthenia)	<i>Muqawwī-i- Aām</i> (General tonic)	3-5gm	Semi-solid preparation	16,17
Majoon Asal-e-Baladur	<i>Du’f-i-Asāb</i> (Nervine weakness)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	3-5gm	Semi-solid preparation	17
Majoon Azaraqī	<i>Du’f-i-Asāb</i> (Nervine weakness), <i>Sar’</i> (Epilepsy)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	3-5gm	Semi-solid preparation	16,17
Majoon Baladur	<i>Du’f-i-Asāb</i> (Nervine weakness), <i>Nisyān</i> (Dementia)	<i>Muqawwī-i- Asāb</i> (Nervine tonic), <i>Muqawwī-i- Dimāgh</i> (Brain tonic), <i>Muqawwī-i- Aām</i> (General tonic)	5-10gm	Semi-solid preparation	16,17
Majoon Falasafa	<i>Nisyān</i> (Dementia)	<i>Muqawwī-i- Aām</i> (General tonic)	5-10gm	Semi-solid preparation	13,17
Majoon Jograj Gugal	<i>Du’f-i-Asāb</i> (Nervine weakness), <i>Ra’sha</i> (Tremor)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	5-10gm	Semi-solid preparation	13,16,17
Majoon Khadar	<i>Du’f-i-Dimāgh</i> (Cerebrasthenia), <i>Du’f-i-Asāb</i> (Nervine weakness), <i>Waram-i-Asāb</i> (Neuritis)	<i>Muqawwī-i- Asāb</i> (Nervine tonic), <i>Muharrīk-i- Asāb</i> (Nervine stimulant)	5-10gm	Semi-solid preparation	13,17
Majoon Lana	<i>Du’f-i-Asāb</i> (Nervine weakness), <i>Ra’sha</i> (Tremor), <i>Sar’</i> (Epilepsy)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	3-5gm	Semi-solid preparation	17
Majoon Mujarrab	<i>Malikhūliya</i> (Melancholia)	<i>Munaqqī-i- Dimāgh</i> (Brain cleanser)	5-10gm	Semi-solid preparation	17
Majoon Muluki	<i>Du’f-i-Asāb</i> (Nervine weakness)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	5-10gm	Semi-solid preparation	17
Majoon Najah	<i>Malikhūliya</i> (Melancholia)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	5-10gm	Semi-solid preparation	16,17
Majoon Nisyān	<i>Nisyān</i> (Dementia)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	5gm	Semi-solid preparation	17
Majoon Seer Alvi Khan	<i>Fālij</i> (Hemiplegia), <i>Ra’sha</i> (Tremor)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	5-10gm	Semi-solid preparation	16,17
Majoon Talkh	<i>Fālij</i> (Hemiplegia), <i>Sar’</i> (Epilepsy)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	5-10gm	Semi-solid preparation	17
Mufarreh Barid	<i>Du’f-i-Asāb</i> (Nervine weakness)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	5-10gm	Semi-solid preparation	16,17
Sharbat Ahmad Shahi	<i>Malikhūliya</i> (Melancholia)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	25-35ml	Syrup	13
Tiryqa Samania	<i>Ra’sha</i> (Tremor), <i>Sar’</i> (Epilepsy), <i>Laqwa</i> (Bell’s palsy)	<i>Muqawwī-i- Asāb</i> (Nervine tonic)	3-5gm	Semi-solid preparation	17

Table 3. Scientific validation studies carried out on Unani Compound formulations for the treatment of various diseases

Unani Polyherbal Formulations	Dose	Therapeutic Uses in Unani	Scientific validation studies	Reference
Majun Falasafa	5-10gm [Nfum 125]	<i>Nisyān</i> (dementia)	Increased life span, Reduction in oxidative stress markers, Protects dopaminergic neurons.	99
Majun Baladur	5-10gm [Nfum 122]	<i>Duʿf-i-Āṣab</i> (Nervine weakness), <i>Nisyān</i> (dementia)	Shown a noteworthy amelioration in neurobehavioral functions in the drug pre-treated rats relative to the ischemic group, as demonstrated by the Rota-Rod, grip strength test, and video path analysis.	100
Majun Baladur	5-10gm [Nfum 122]	<i>Duʿf-i-Āṣab</i> (Nervine weakness), <i>Nisyān</i> (dementia)	Protects dopaminergic neurons, increased life span, Reduction in oxidative stress markers.	101
Khamira Abresham Hakim Arshad Wala	5g [Nfum 75]	<i>Duʿf-i-Umūmi</i> (General tonic), <i>Duʿf-i-Ādaʾ Raʿisa</i> (General debility), <i>Malankhuliya</i> (melancholia)	Antioxidant and helps improving cognitive function and neurobehavioral activities.	102
Majun Najah	5-10g [Nfum 138]	<i>Duʿf-i-Āṣab</i> (Nervine weakness), <i>Malankhuliya</i> (melancholia), <i>Ikhitnaq-ur-reham</i> (Hysteria)	Significant anticonvulsant activity, Anti-depressant activity	103,104
Sharbat-e-Ahmed Shahi	25-35ml	<i>Malankhuliya</i> (melancholia), <i>Māhiyā</i> (Psychosis), <i>Duʿf-i-Dimāgh</i> (Cerebral insufficiency)	Antidepressant and anxiolytic effect by increasing the levels of serotonin.	105
Itrifal Muqawwi-e-Dimagh	5-10g [Nfum 64]	<i>Duʿf-i-Dimāgh</i> (Cerebral insufficiency)	Shown reduction in PD symptoms being mimicked in transgenicFlies	(Siddique et al., 2021a)
Majoun Saranjan	5-10g [Nfum 144]	<i>Waja-ul-mafasil</i> (Polyarthritis), <i>Niqris</i> (Gout), <i>Waram-i-Mafasil</i> (Arthritis)	Inhibited the delayed increase in joint diameter as seen in control and aspirin treated animals in Freund's adjuvant induced arthritis.	(Singh et al., 2011)
Jawarish Zaronni Sada	5-10g [Nfum 106]	<i>Duʿf-i-kulya</i> (Renal insufficiency), <i>Hasat-i-kulya</i> (Renal calculi)	Diuretic and nephroprotective effect.	106
Habb-e-Asgand	2 pills (each 650mg) [Nfum8]	<i>Waja-ul-mafasil</i> (Polyarthritis), <i>Wajaʾ al-Warik</i> (Coccydynia)	Anti-arthritic activity.	107
Safoof Mohazzil	5-10g [Nfum 239]	<i>Saman-i-mufrif</i> (Obesity)	Antioxidant and anti-inflammatory.	108
Qurs Tabasheer	2 pills	<i>Dhayabitus</i> (diabetes)	Anti-hyperglycemic, anti-hyperlipidemic in STZ- induced wistar rat.	109
Habbe Gule Aakh	250mg [Nfum 15]	<i>Waja-ul-mafasil</i> (Polyarthritis), <i>Waram-i-Mafasil</i> (Arthritis)	Anti-inflammatory and analgesic.	110
Qalbeen- A polyherbal mineral formulation	2 pills [Nfum24]	<i>Khafaqan</i> (Palpitation), <i>Duʿf-i-Qalb</i> (Cardiac insufficiency)	Effective against Ischaemic heart disease (IHD).	111
Qurs Tabasheer	2 pills	<i>Dhayabitus</i> (diabetes)	Antidiabetic, Anti-hyperlipidaemic & Hepatoprotective.	112
Majoon-e-Dabeed-ul-ward	5-10g [Nfum183]	<i>Itisqaʾ</i> (Oedema), <i>Duʿf-i-kabid</i> (Hepatic insufficiency), <i>Waram-i-kabid</i> (Hepatitis), <i>Faqr al-Dam</i> (Anaemia)	Hepatoprotective effect.	113
Khamira Abresham Hakim Arshad Walaʾ	3-6g [Nfum108]	<i>Khafaqan</i> (Palpitation), <i>Duʿf-i-Ādaʾ Raʿisa</i> (General debility)	Cardioprotective and potential against isoproterenol induced myocardial necrosis and associated oxidative stress.	114
Jawarish-e-Amla Sada	5-10g [Nfum- 97]	<i>Duʿf-i-kabid</i> (Hepatic insufficiency), <i>Duʿf-al-Midaʾ</i> (Gastric insufficiency), <i>khafaqan</i> (Palpitation), <i>Duʿf al-Qalb</i> (Cardiac insufficiency)	Hepatoprotective effect and potential to provide protection against toxic effects of cyclophosphamide in tumour bearing mice.	115

Table 4. Antioxidant/ Memory enhancing/ Anti depression/ Immunomodulatory activities of the proposed herbs

Unani Name (Scientific Name)	Common name	Family	Active constituent	Pharmacological activity	Reference
Amla (<i>Phyllanthus emblica</i> L.)	Amla	Phyllanthaceae	Emblcannin A & B, Alkaloid (Phyllantine), Phenol (Gallic acid)	Antioxidant	37
Anjeer (<i>Ficus carica</i> L.)	Fig	Moraceae	Phenols	Antioxidant	116
Aqar qarba (<i>Anacyclus pyrethrum</i> (L.) Lag.)	Pellitory	Asteraceae	Anacyclin	Antioxidant, Memory enhancer, Anti-depressant	55,63
Asaroon (<i>Asarum europaeum</i> L.)	Hazelnut	Aristolochiaceae	Essential oils, Volatile oil, caffeic acid, flavonoids	Neuroprotective, Antioxidant	117
Asgand (<i>Withania Somnifera</i> (L.) Dunal.)	Winter Cherry	Solanaceae	Withanine, Somniferine	Antioxidant	21
Azāraqī (<i>Strychnos nux-vomica</i> L.)	Kuchla	Loganiaceae	Strychnine, Brucine	Antioxidant, Anti-amnesic, Anti-convulsant	118,119
Badam Shirin (<i>Prunus amygdalus</i> Batsch.)	Almond	Rosaceae	Amandine	Antioxidant, Memory-enhancer	22,56
Badranjboya (<i>Nepeta hindostana</i> Haines)	Catmint	Lamiaceae	Hydrocarbons (Sesquiterpene)	Antioxidant	23,24
Balela (<i>Terminalia bellirica</i> Roxb.)	Bahera	Combretaceae	Beta-sitosterol, gallic acid, ellagic acid, bellaricin	Antioxidant, Anti-Alzheimer's, Anti-depressant	25,45,64
Bazz-ul-Banj (<i>Hyoscyamus niger</i> L.)	Henbane	Solanaceae	Hyoscyamine, hyosine, Scopolamine	Antioxidant, Anti-depressant, Anti-parkinsonism	26,51,65,120
Bisbāsa (<i>Myristica fragrans</i> Houtt.)	Mace, Javitri	Myristicaceae	Terpenoids, phenols	Antioxidant, Memory-enhancer, Anti-Alzheimer's	34,46
Brahmi (<i>Bacopa monnieri</i> (Linn.) Pennel.)	Water hyssop	Scrophulariaceae	Bacoside, brahmin, herpestine, d-mannitol, luteolin, apigenin	Antioxidant, Memory-enhancer, Anti-depressant, Anti-Alzheimer's, Anti-parkinsonism, Neuroprotective	27,47,53,66
Darchini (<i>Cinnamomum verum</i> J. Presl)	Cinnamon	Lauraceae	Cinnamic acid, Cinnamate	Antioxidant, Anti-parkinsonism, Anti-depressant	28,54,121
Filfil Daraz (<i>Piper longum</i> L.)	Long pepper	Piperaceae	Piperine	Antioxidant, Anti-depressant	29,67
Filfil Siyah (<i>Piper nigrum</i> L.)	Black & White Pepper	Piperaceae	Piperine, Piperidine	Antioxidant, Neuroprotective	77,122
Gurmar (<i>Gymnema sylvestre</i> R. Br.)	Gymnema	Apocynaceae	Gymnemic acids, Gymnemasides, Gymnemenol	Antioxidant	30
Halela Zard (<i>Terminalia chebula</i> Retz.)	Harad	Combretaceae	Pyrogallol, chebulinic acid, ellagic acid	Antioxidant	31,123
Jadwar (<i>Delphinium denudatum</i> wall.)	Blood veined sage	Ranunculaceae	Flavonoids, Triterpenoids, Alkaloids	Antioxidant, Anti-Alzheimer's, Anti-depressant, Anti-anxiety, Anti-convulsant	32,48,68,124
Jawz (<i>Juglans regia</i> L.)	Walnut	Juglandaceae	Juglandic acid, Juglone, Juglone	Antioxidant, Memory enhancer, Anti-depressant	33,58
Jawzbawa (<i>Myristica fragrans</i> Houtt.)	Nutmeg	Myristicaceae	Fixed oil, Volatile oil, lignan	Antioxidant, Anti-depressant, Anti-convulsant	34,70,125
Kababa (<i>Piper cubeba</i> L.f.)	Tailed pepper	Piperaceae	Essential oil	Antioxidant	126
Khulanjan (<i>Alpinia galanga</i> Willd.)	Siamese ginger	Zingiberaceae	Flavonoids, triterpenes	Antioxidant	35
Kundur (<i>Boswellia serrata</i> Triana & Planch.)	Olibanum	Burseraceae	Essential oil, Terpenoids, Boswellic acids (BAs)	Anti-Alzheimer's, Neuroprotective	75
Mastagi (<i>Pistacia lentiscus</i> L.)	Lentisco	Anacardiaceae	Terpinene, Flavonoids	Antioxidant	36
Muqil (<i>Commiphora wightii</i> Bhandari)	Gum guga	Burseraceae	Terpenoids, Flavonoids	Antioxidant	127
Qust Shirin (<i>Saussurea lappa</i> CB Clarke.)	Costus root	Asteraceae	Phenols, Flavonoids	Antioxidant, Anti-Alzheimer's	128,129
Ratab (<i>Phoenix dactylifera</i> L.)	Dates	Areaceae	Phenols, Flavonoids, tannins	Antioxidant, Prevention of peripheral neuropathy activity	38,130
Rehan (<i>Ocimum tenuiflorum</i> L.)	Holy Basil	Lamiaceae	3,4-dimethoxycinnamic acid, Pedunculin	Antioxidant, Memory enhancer, Anti-anxiety, Anti-depressant, Anti-convulsant	60,71,131
Rumman (<i>Punica granatum</i> L.)	Pomegranate	Lythraceae	Punicalin, Punicallagine	Antioxidant	39
Shoneez (<i>Nigella sativa</i> L.)	Black Cumin	Ranunculaceae	Nigellidine, Nigelline, thymoquinone	Antioxidant	132
Seer (<i>Allium sativum</i> L.)	Garlic	Liliaceae	Ajoenes, thiosulfates, allin, allicin	Antioxidant, Anti-Alzheimer's	49,133
Sumbul ut-teeb (<i>Nardostachys jatamansi</i>)	Broomroot	Caprifoliaceae	Sesquiterpenes, coumarins, valeranone, jatamansone	Antioxidant, Stress-relieving activity	40,134
Ustukhuddus (<i>Lavandula stoechas</i> L.)	broom of the brain	Lamiaceae	glycosides, phenols,terpenes	Anti-amnesic	135
Waj turki (<i>Acorus calamus</i> L.)	Sweet flag	Araceae	Volatile oils, flavonoids, phenols	Antioxidant, Memory enhancer	136,137
Zafran (<i>Crocus sativus</i> L.)	Saffron	Iridaceae	Crocin, picrocrocin, crocetin	Antioxidant, Anti-Alzheimer's, Memory enhancer	41,50,61,62
Zaitoon (<i>Olea europaea</i> L.)	Olive	Oleaceae	Secoiridoids, terpenoids	Antioxidant	42
Zanjabeel (<i>Zingiber officinale</i> Roscoe)	Ginger	Zingiberaceae	Terpenes, Phenols, Essential oils, Oleoresin (Gingerol, shogaol, zingerone)	Antioxidant, Neuroprotective, Cognitive enhancer activity	80-82,138
Zard Chob (<i>Curcuma longa</i> L.)	Turmeric	Zingiberaceae	Curcumin	Antioxidant, Anti-depressant	44,73,74

dose, dosage form, and important formulations is presented in Table 1. All the single herbs presented have pharmacological activities associated with the treatment of NDDs, such as antioxidant, anti-Alzheimer's, anti-Parkinsonism, anti-depressant, anti-convulsant, anti-anxiety, neuroprotective, and memory enhancer activities (Figure 1) and (Table 4).

Polyherbal Formulations. In Unani classical texts, a number of compound formulations are mentioned only 39 polyherbal formulations are discussed here for the treatment of brain disorders. The data is given in (Figure 2). The dosage

forms for these compositions include *habb* (pills), and semi-solid preparations such as *itrifal*, *khamira*, *maʿjuʿn*, and *jawarish*. These dosage forms come in a variety of textures and processing techniques. The majority of the formulations have been suggested for oral use. Unani compound formulations are recommended to patients not only for the treatment of neurological disorders but also for other ailments such as *Waram-i-Mafasil* (Arthritis), *Duʿf-i-Qalb* (Cardiac insufficiency), *Waram-i-kabid* (Hepatitis), *Faqr al-Dam* (Anaemia) etc. The need of the hour is to validate

Figure 1. This bar graph illustrates the various pharmacological activities of the studies Unani drugs.

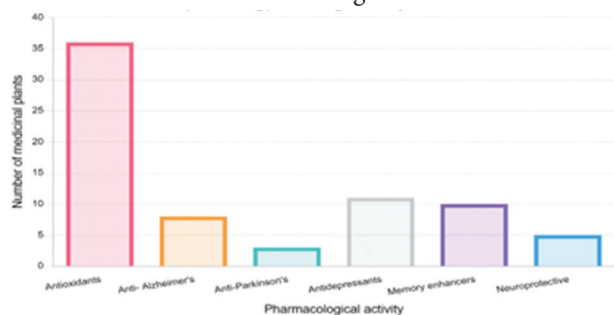
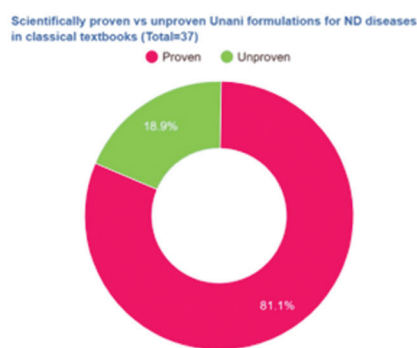


Figure 2. Scientifically proven = 7 Unproven = 30



Unani single drugs, as well as compound formulations for their therapeutic and adverse effects, which is a dire necessity. The compound formulations advocated in Unani medicine for the treatments of brain illnesses are listed in Table 2, and the studies that have been carried out so far on a few of these formulations to date as per the record in Google Scholar (www.google scholar.com) to validate them and characterize their effects are listed in Table 3.

Mechanisms by which Unani medicines treat Neurodegenerative disorders

From Unani perspective, the efficacy of mentioned herbs and compound formulations in the treatment of NDDs may be attributed to their *Muqawwi-i-Asāb* (Nervine tonic), *Muqawwi-i-Dimāgh* (Brain tonic), *Muqawwi-i-Hāfizā* (Memory enhancer), *Muḥarrrik-i-Āṣāb* (Nervine stimulant), *Munaqqf-i-Dimāgh* (Brain cleanser), *Mukhrij-i-Rutūbāt* (Morbid matter remover) properties. However, from an allopathic perspective, it can be explained by the following mechanisms: (i) Antioxidant, (ii) Memory enhancing activity, (iii) Anti-Alzheimer's activity, (iv) Anti-Parkinson's activity, (v) Anti-depressant activity, (vi) Anti-anxiety, and (vii) Neuroprotective activity of the drugs. In USM, most NDDs occur when *yubuṣat* (dryness) predominates in the body, causing the *jawhar* (essence) of the organ to disintegrate and destroy, resulting in organs becoming weak and unable to perform their functions, as we have seen in conventional medicine when the aging process starts⁹ and degenerative changes seen due to oxidative stress. As a result, neuroprotective herbal antioxidants are considered an

effective approach to slowing the progression of various illnesses and reducing the degree of neuronal cell death. The pharmacological evidence of the activities of the proposed herbs for the treatment of NDDs is described below.

Antioxidant activity. A study evaluated that the Gallic acid equivalent as total phenolic content from the fruit of *Āmla* has excellent antioxidant activity.¹⁸ Many studies for *W. somnifera* conducted on rat's brains showed the herb produced an increase in the levels of three natural antioxidants-superoxide dismutase, catalase, and glutathione peroxidase. This effect may explain the reported anti-stress, cognition-facilitation, anti-inflammatory, and anti-ageing effects produced by them in experimental animals, and clinical evaluation¹⁹⁻²¹ A study concluded that methanolic extract of *P. amygdalus* may help to prevent or slow the growth of various oxidative stress-related diseases.²² The oil of *N. hindostana* showed a significant effect in inhibiting free radicals produced by DPPH, reaching up to 73.4% at 60 μL and IC₅₀ value was found as 8.5 μL. This capacity was decreased with a decrease of oil concentration 40 (72.82), 20 (64.09), 10 (52.46), and 5μL (32.79%).^{23,24} The antioxidant activity of *T. bellerica* has been reported by Kumari et al., 2017.²⁵ Water extracts of *H. niger* showed radical scavenging, anti-oxidant capacity, ferric, and cupric-reducing powers.²⁶ The extract of *B. monnieri* possesses anti-oxidant, anti-stress, cognition-facilitating, and anti-aging effects.²⁷ Various studies have confirmed that 26 species of *C. verum* showed the highest antioxidant activity.²⁸ Piperine from *Piper longum* maintains glutathione content demonstrating anti-oxidant activity.²⁹ *G. sylvestre* was found to have significant radical scavenging activity against ferric ($P < .05$), super oxide ($P < .05$), and also against hydrogen peroxide ($P < .05$).³⁰ The leaves, barks, and fruit of *T. chebula* possessed high antioxidant activity and phenolics were found to be responsible for this.³¹ *D. denudatum* aqueous root extract has antioxidants and could offer a promising role in the treatment of nephrotoxin-induced renal injury such as cisplatin.³² A study reported a decrease in the antioxidant burden observed in enzymatic and non-enzymatic antioxidant systems after consumption of a whole walnut (*J. regia*) diet in C57BL/6 mice.³³ The high antioxidant activity of *M. fragrans* was reported by Jukić et al., 2006.³⁴ The ethanol extract of *A. galanga* has the highest free radical DPPH neutralizing ability.³⁵ Aqueous extract of *P. lentiscus* contains a high level of phenolic compound and is an effective antioxidant in different assays like DPPH radical, hydrogen peroxide scavenging, reducing power, and total anti-oxidant capacity.³⁶ *O. sanctum* also exhibits antioxidant activity.³⁷ El Abed et al. showed that parthenocarpic dates had strong scavenging activity on DPPH reaching 94% with an IC₅₀ value of 0.15± 0.011 mg/mL ($P < .05$).³⁸ A study reported that Pomegranate extract has been found to scavenge free radicals and increase plasma anti-oxidant capacity in elderly humans.³⁹ A study suggested that *N. jatamansi* unequivocally is a potential source of antioxidants and could aid in alleviating oxidative stress-mediated disorders⁴⁰ Findings have demonstrated that

active and inactive constituents of *C. sativus* extract have high antioxidant activity.⁴¹ A study demonstrated that *O. europaea* fruit extracts can represent an important natural source of antioxidant potential.⁴² Significant antioxidant activity of volatile and non-volatile compounds of fresh and dried *Z. officinale* was noted by using DPPH and ferric reducing antioxidant power.⁴³ The curcumin component of *C. longa* possesses strong antioxidant activity.⁴⁴

Anti-Alzheimer's activity. Anti-Alzheimer's activity of these drugs has been confirmed by various studies. Being an acetylcholinesterase inhibitor, *T. bellerica* could be used for symptomatic treatment of Alzheimer's disease.⁴⁵ In one study, it was found that a hydro-alcoholic extract of Nutmeg did show significant (50%) inhibition of acetylcholinesterase for the treatment of AD.⁴⁶ Goswami et al. 2011 evaluated the anti-Alzheimer's activity of *B. monnieri* after administering 300mg *B. monnieri* (orally) twice a day for 6 months in the newly diagnosed patients of AD.⁴⁷ Ahmad et al. 2017 investigated the impact of *D. denudatum* extract on neuronal injury and hence proved that it can be used in AD as a target drug.⁴⁸ Akinyemi et al. 2018 evaluated that Oil from garlic bulbs suppressed AChE activity of cerebral cortex synaptosome and exhibited antioxidant properties.⁴⁹ AD was characterized pathologically by the deposition of amyloid beta-peptide (Aβ) fibrils. Possible use of *C. sativus* stigma constituents for inhibition of aggregation and deposition of Aβ in the human brain.⁵⁰

Anti-Parkinson activity. Several studies have reported the anti-Parkinson activity of the proposed herbs. Aqueous methanol extract of *H. niger* seeds significantly attenuated motor disabilities (akinesia, catalepsy, and reduced swim score) and striatal dopamine loss in methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine treated mice and also against the stereotaxically induced rotenone model of Parkinson's disease in rats due to antioxidant activity.⁵¹ Jadiya et al. 2011 studied the effect of *B. monnieri* and proved that *B. monnieri* reduced alpha synuclein aggregation, prevented dopaminergic neurodegeneration and restored the lipid content in nematodes, thereby providing its potential as a possible anti-Parkinsonian agent.⁵² Swathi et al. 2013 also examined the neuroprotective effect of *B. monnieri* in rotenone-induced Parkinson's disease with particular reference to glutamate metabolism in different regions of the rat brain. The results suggest the ability of *B. monnieri* extract to modulate glutamate metabolism in different brain regions of the induced rodent model of PD.⁵³ PD protein 7 (PARK7) is an autosomal recessive form of early-onset Parkinsonism caused by alterations in the DJ1 gene. Khasnavis and Pahan reported that sodium benzoate, a cinnamon metabolite, upregulates DJ-1 by modulating mevalonate metabolites. In the CNS of the mouse, cinnamon and its metabolite sodium benzoate additionally rise the levels of neurotrophin-3 (NT-3) and brain-derived neurotrophic factors (BDNF).⁵⁴

Memory enhancing activity. A study suggests that ethanolic extract of *A. pyrethrum* increased brain cholinergic levels and hence it possesses memory-enhancing activity in

scopolamine-induced amnesia model by enhancing central cholinergic neurotransmission.⁵⁵ In one study nootropic effects of almonds were evaluated in rat models and found that a significant improvement in learning and memory of almond-treated rats was reported compared to control.⁵⁶ Polyphenolic extracts from Walnut testa (42%) improved learning and memory functions in hypercholesterolemic mice based on obesity, hypercholesterolemia, and oxidative stress.⁵⁷ Recently researchers proved that dietary supplementation with walnuts 6% or 9% improved learning skills, memory, anxiety, locomotor activity, and motor coordination in the Tg2576 transgenic mouse model of Alzheimer's disease.^{58,59} Alcoholic extract of *O. sanctum* ameliorated the amnesic effect of scopolamine (0.4 mg/kg) and aging-induced memory deficits in mice. Hence, *O. sanctum* can be employed in the treatment of cognitive disorders such as dementia and AD.⁶⁰ Saffron extract or its active constituents crocetin and crocin could be useful as a treatment for neurodegenerative disorders accompanying memory impairment.^{61,62} A study suggested that *Z. officinale* extract is a potential cognitive enhancer for middle-aged women.⁴³

Anti-depressant activity. *A. pyrethrum* root extract produces a significant anti-depressant effect.⁶³ An investigation was carried out to study the anti-depressant activity of *T. bellerica* extract and concluded that it exhibits a significant anti-depressant effect.⁶⁴ Patil et al. proved the anti-depressant activity of *H. niger* extract.⁶⁵ A study demonstrated that *B. monnieri* extract containing 25% bacoside A exerted anxiolytic activity comparable to Lorazepam (anxiolytic drug).⁶⁶ Ethanol extract of *P. longum* represents a promising pharmacotherapeutic candidate as an anti-depressant agent.⁶⁷ Zafar et al. evaluated the central depressant activity of the aqueous extract of *D. denudatum*.⁶⁸ The macerated hexane extract of *J. regia* fruit produced significant anti-depressant activity.⁶⁹ N-hexane extract of *M. fragrans* Houtt. elicited significant anti-depressant-like effect.⁷⁰ A study showed that extracts of *O. sanctum* show anti-anxiety and anti-depressant properties.⁷¹ A study suggests that *N. jatamansi* has dose-dependent anti-depressant activity and can be used in patients suffering from depression due to sleep disturbances.⁷² Some studies also showed that Curcumin of *C. longa* has anti-depression properties.^{73,74}

Neuroprotective activity. The active constituents of *B. monnieri* is responsible for cognitive effects are bacosides A and B, moreover triterpenoid saponins are responsible for enhancing nerve impulse transmission.⁷⁵ The bacosides also aid in the repair of damaged neurons by enhancing kinase activity, neuronal synthesis, restoration of synaptic activity, and nerve impulse transmission.⁷⁶ Piperine of *P. nigrum* increases cell viability and restores mitochondrial functioning and primary neurons in rotenone-induced neurotoxicity in SK-N-SH cells. It also inhibits Mtorc1 and activates protein phosphatase 2A, leading to neuroprotective effects in Parkinson's disease model.⁷⁷ Another study described the neuroprotective activity of a 6% walnut diet against

neurotoxicity in male rats induced by the anti-cancer drug cisplatin.⁵⁹ *Boswellia* species and their active constituents BAs have been thoroughly investigated for their possible role in neuroprotection owing to their anti-inflammatory actions.^{78,79} An important study has shown that 6-shogaol of *Z. officinale* has neuroprotective effects in transient global ischemia via the inhibition of microglia.^{80,81} Another finding in the support of ginger as neuroprotective suggests that it exhibits neuroprotective effects by accelerating brain antioxidant defense mechanisms and down-regulating the MDA levels to the normal levels in diabetic rats.⁸²

DISCUSSION

In Unani medicine, Neurodegenerative disorders have been described under the heading of *Amrād-i-ʿAshāb* (Nervous disorders) and *Amrād-i-Dimāgh* (Brain disorders), wherein *Rʿsha* (tremors), *Nisyān* (dementia), *Fālij* (paralysis), *Saktā* (apoplexy), etc have been explained elaborately.^{10,11}

The Mizāj of brain is described as cold and wet, making it particularly susceptible to various stimuli.⁸³ When a disorder affects the entire brain, all of its Quwā (faculties) are collectively impacted. Conversely, partial brain disorders affect specific Quwā or the nerves originating from those affected areas.^{9,84} For example, a disease impacting the frontal part of the brain disrupts Quwwat-i-Takhayyul (faculty of imagination), while mid-brain disturbances affect Quwwat-i-Fikr (faculty of thought), and issues with Quwwat-i-Zikr (faculty of memory) are observed when the hindbrain is affected.

Oxidative stress can be conceptualized as Ihtirāq (burnout) of Khilt (temperament) or the increased production of Fudlāt (waste products) due to weakened Quwwat Ghāziya (vital force) and Quwwat Dafīʿa (, leading to the accumulation of more Fudlāt in the body as we age. In conventional medicine ageing occurs when cells become permanently damaged from the lifelong and unrelenting attack of charge molecule fragments, known as free radicals e.g. H₂O₂, O₂, lipid peroxidation, nitric oxide, result of autooxidation such as Fe²⁺, Cu²⁺ ascorbic acid glutathione flavin co-enzymes. Finally 80-90 per cent of all degenerative diseases are now believed to involve free radical activity. Healthy ageing and maximum longevity may depend on the genetic makeup of an organism under strict control by nature and nurture. In this context Unani medicine addresses the concept of Asbāb Sittā Darūriya. Complying of these essential factors delayed ageing by maintaining Rutūbat Gharīziyya and Ḥararat Gharīziyya at desired quantum. These are achieved merely by preservation of Rutūbat Gharīziyya because in vice versa Rutūbat Gharība predominates over the body thereby the natural Ḥār raṭb temperament of the body changes to Bārid Yābis.

When Yubūsat predominates in the body, it causes the Jawhar (essential material) of organs to disintegrate and weaken, resulting in fragile organs that cannot perform their functions effectively, akin to the concept of degenerative disorders in conventional medicine that manifest with aging.⁹ Another aspect is when Quwwat Tabīʿiyya (natural power) is weakened, it leads to inadequate production of Rutūbat

Gharīziyya (vital moisture), which is crucial for sustaining Harārat Gharīziyya (vital heat). This imbalance affects all faculties, or vice versa, leading to an accumulation of harmful substances in the body, similar to the theory of free radicals. Strategies such as scavenging effects are employed to prevent the detrimental effects caused by free radicals.

Oxidative stress serves as a precursor to the formation of amyloid plaques and tau protein aggregation, which are repeated throughout life and are outcomes of Khilt Ihtirāq (temperamental burnout). By maintaining Rutūbat Asliyya (primary moisture) through adherence to Asbāb Sittā Darūriya (six essential factors), the onset of Khilt Ihtirāq can be prevented. Furthermore, disturbances in energy production occur when essential enzymes necessary for mitochondrial energy production are insufficient, despite the presence of oxygen and nutrients. This deficiency is attributed to the inadequate availability of fluids that facilitate enzyme function. Mitochondrial dysfunction is implicated in various neurological and muscular disorders associated with aging. ref. Interaction between specific enzyme and protein channel plays crucial role in mitochondrial function.⁸⁵ Unani medicine differs for conventional medicine in diagnostic and therapeutic approaches because both are differed to the handling of the human body based on holism and reductionism approaches respectively. In the diagnostic approach Mizāj of a person, Mizāj of disease, Mizāj of season, Mizāj of habitat, understating of Nabd and inspection of Bawl are required. For therapeutic approaches Mundij and Mushil therapy, Eʿitidal Mizāj, Muqawwiyaṭ (tonics), Muraṭtibāt (humectant) and dietary modification are the basic principles of treatment. Whereas in conventional medicine hematological, radiological and some memory identifying tools are the basic practices for devising investigation. For therapeutic approach antioxidant as well as symptomatic treatments are the basic form of treatment. It is inferred that Unani therapy is apparently more robust, holistic and inclusive because it cleanses the lodging morbid matters as well as strengthening to the organs by moisturising, made to equable temperaments of the organs, reformation of liver (the original source of production of Akhlāt) and dietary modification as needed.

Recent studies have revealed that autophagy, apoptosis, oxidative stress, and neuroinflammation are important components of the pathogenesis of NDDs. Among these apoptosis mediated by mitochondrial dysfunction is unavoidable.⁸⁶ The production of cellular energy is carried out by mitochondria, which are also thought to contribute to aging and NDDs. Research conducted in living organisms has demonstrated that certain herbs with “tonifying” effects may enhance the production of mitochondrial ATP in a variety of tissues, including the rat brain e.g., *Asgand* (*Withania somnifera*), *Azaraqi* (*Strychnos nux vomica*), etc.²¹ These herbs may also increase the activities of mitochondrial antioxidant components.^{87,88} As a cell with a high demand for energy, neurons have a strong dependence on mitochondria. Therefore, proper maintenance of mitochondrial function is

critical for neuronal cells and is a potential therapeutic target for neurodegenerative diseases such as AD, and PD. Unani scholars have already categorized the functions of many herbs as *Muqawwi-i-dimāgh wa A'sāb* (Brain and nerve tonic). It is inferred that said herbs exert 'tonifying' effects on the brain and nervous tissues. In recent years, OS and the generation of ROS have been recognized as fundamental pathologies impinging at least partially on several age-related disorders including NDDs. The oxidative stress hypothesis suggests that the brain remains healthy as long as 'free radicals' that are produced in the course of the various biochemical reactions in the body are kept in check by 'antioxidants'.^{89,90} and in this article, we found 43 single herbs having potent antioxidant properties seen in Table 4.⁹ The mechanism by which Unani drugs work to prevent or delay the progression of NDDs is by offering their functions as brain tonics, and nerve tonics e.g., *Badām Shirīn* (*Prunus amygdalus*), *Anjīr* (*Ficus carica*), *Zaitūn* (*Olea europaea*), *badranjboya* (*Melissa officinalis* L), *Prunella vulgaris* L, *Barahmi* (*Centella asiatica* L), *Za 'faran* (*Crocus sativus* L), *Kutki* (*Picrorhiza kurroa* Royle ex Benth), *Khamīra banafsha Kashmirī*, *Roghan chanbelī*, etc. by maintaining the moisture of the nerve fibers. Another mechanism of treating NDDs in Unani medicine is to expel superfluous matter from the brain produced in the course of NDDs and this can be seen by using drugs having *Munaqqī-i-Dimāgh* (brain cleanser) and *Mukhrij-i- Rutubat* (morbid matter remover) properties like *Waj Turki* (*Acorus calamus* L.), *Ustukhuddūs* (*Lavandula stoechas* L.), *Halīla Kābulī* (*Terminalia chebula* Retz.), *Zanjabīl Khushk* (*Zingiber officinale* Rose), etc.^{10,12} Similarly, conventional medicine considers the aforementioned action to be the scavenging actions of several drugs by reducing amyloid deposits or plaque formation as observed in AD. Some Unani drugs e.g., *Bādranjboya* (*Nepeta hindostana* (Roth.) Haines), *Ud Salīb* (*Paeonia emodi*), *Bīkh Izkhār* (*Cymbopogon martini*), *Kuchla* (*Strychnos nux vomica*), *Maghz Chilghoza* (*Pinus gerardiana*), *Sibr* (*Aloe barbadensis*), *Roghan Badām Talkh* act by exerting the action as *Muḥallil* (anti-inflammatory) in treating various forms of NDDs.^{11,12,91} Numerous natural herbs with varying origins have been suggested as treatments for neurodegenerative diseases because of their neuroprotective properties. It has been shown that they do not only target symptoms but also account several facets of the pathophysiology of the disease.⁹² Several natural compounds, extracts, and herb formulae have been thoroughly researched against numerous NDDs, with positive results. Alkaloids, phenylpropanoids, polyketides, and terpenoids are the four classes of natural substances based on their origin. *Alkaloids* are a class of naturally occurring organic nitrogen-containing compounds.^{93,94} They have anti-inflammatory, antioxidant, anticancer, analgesic, antibacterial, and antifungal properties are found in many plants e.g., Withanine, somniferine, amandine, scopolamine, piperine, and other alkaloids extracted from proposed Unani herbs have been studied for their medicinal potential in the treatment of neurodegenerative illnesses. *Phenylpropanoids*,

often known as cinnamic acid, are a class of aromatic organic compounds. *Phenylpropanoids* can be further classified into five groups namely flavonoids, lignins, phenolic acids, stilbenes, and coumarins.⁹⁵ Because of their antioxidant and anti-inflammatory properties, *phenylpropanoids* such as curcumin of *Zard chob* (*Curcuma longa* L.) have sparked a lot of interest in the treatment of neurological conditions in recent years. Terpenoids, also known as isoprenoids, are the most abundant class of natural substances, accounting for over 60% of all known molecules. They are found mostly in plants, microbial sources, and marine sponges.⁹⁶ Numerous NDDs have aberrant protein dynamics, impaired degradation, oxidative stress and the production of ROS, mitochondrial dysfunction, DNA damage, and neuroinflammatory and neuroimmune processes as their primary etiology. These processes interact with one another in intricate feedback loops that ultimately cause cell malfunction and death.⁹⁷ The authors examined the uses and purposes of Unani medicine having these natural substances for the treatment of NDDs. The use of Unani medicine therapy has demonstrated promising antioxidant, memory enhancer, antidepressant, anti-Alzheimer's, and anti-Parkinson's activities that may have a positive impact on slowing the progression of NDDs (table 4). For example, *Asgand* (*W. somnifera*) is a potent antioxidant drug that increases the levels of three natural antioxidants- superoxide dismutase, catalase, and glutathione peroxidase. This impact might explain the anti-stress, cognitive facilitation, anti-inflammatory, and anti-ageing benefits shown in clinical investigations.^{19,21}

On account of the limitations and severe side effects of allopathic therapies for neurodegenerative illnesses, traditional medicines particularly Unani medicine may be a viable alternative. Several plant-derived compounds used in Unani medicine may be helpful in forthcoming research, particularly neurological problems. Through various single and compound formulations that act as antioxidants and neuroprotective and reduce amyloid deposits, anti-inflammatory, and immunomodulating that alter neuroendocrine-immune activities, improve memory, activate neurofunctions, and improve quality of life.

CONCLUSION

There are various single herbs and compound formulations in the Unani system of medicine for the treatment of NDDs as most plant-derived compounds have antioxidant, anti-amnesic, anti-Alzheimer's, and antidepressant activities. Several of them have shown efficacy in clinical studies. These studies suggested that administering herbal formulations considerably improves symptoms of neurodegenerative illnesses such as tremors, dementia, depression, psychosis, postural instability, etc. The mechanism by which Unani medicine works is ratified by various in-vitro and in-vivo studies. As a result, scientifically validated Unani formulations can be suggested in clinical practice for the treatment of NDDs.

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