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Unraveling The Neurotherapeutic Potential of *Mahakalyanaka Ghrita* In Non-Motor Dimensions Of Parkinson's Disease

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ABSTRACT

Parkinson's disease (PD) is commonly associated with motor symptoms, but Non-motor features such as cognitive decline, mood disorders, sleep disturbances, and autonomic dysfunction significantly affect patients' quality of life. These non-motor symptoms often remain underrecognized and inadequately treated. *Mahakalyanaka Ghrita*, an *Ayurvedic* formulation combining ghee with medicinal herbs, is traditionally used to address neurological disorders. This conceptual review explores the potential mode of action of *Mahakalyanaka Ghrita* in managing the Non-motor features of Parkinson's disease. The ingredients in this formulation possess Neuroprotective, Anti-Anti Parkinson's, Inflammatory, Antioxidant, and Adaptogenic properties, which may help alleviate Cognitive dysfunction, Mood disorders, Sleep disturbances, Sexual dysfunctions and Autonomic dysfunction commonly seen in PD. From an *Ayurvedic* perspective, *Mahakalyanaka Ghrita* is believed to balance *tridoshas*, contributing to overall Neurological and Emotional well-being. The review underscores the importance of integrating *Mahakalyanaka Ghrita* as an adjunct to conventional therapies, with a call for further clinical studies to validate its efficacy in managing Non-motor features of Parkinson's disease.

Keywords: Parkinson's disease, Non-motor symptoms, *Mahakalyanaka Ghrita*.

INTRODUCTION

Parkinson's disease is the common age related multisystemic progressive neurodegenerative disorder. Since long the main clinical focus in Parkinson's disease has been on motor symptoms such as Bradykinesia, Rigidity, Tremors, Postural instability, however there is increasing recognition that the clinical spectrum of Parkinson's disease is more extensive, including Non-Motor Symptoms such as variety of Cognitive, Neuro psychiatric, Sleep, Autonomic and Sensory Dysfunctions. Recently Non motor symptoms are recognised as an important part of Parkinson's disease symptoms which is a significant cause of disability and poor quality of life. **(1)** PD is found world-wide and is one of the most common extrapyramidal disorders seen in clinical practice. Epidemiological studies have shown a relatively lesser incidence and crude prevalence of PD in countries like Africa, India and China when compared to Western populations except among the Parsis of India who have a high incidence of the disease. Prevalence of PD in India is estimated to be between 15 and 43 per 1,00,000 people, making it one of the countries with the highest number of PD patients in the world due to India's large population, with an estimated 7 million people with PD. **(2)**

The pathogenesis of Non-motor symptoms in PD is multifactorial, involving a combination of neurodegeneration, neurotransmitter imbalances, and disruptions in the brain's neural circuits beyond the dopaminergic system. While interest has focused more on the dopamine system, but neuronal degeneration with Lewy pathology can also affect cholinergic neurons of the nucleus basalis of Meynert (NBM), norepinephrine neurons of the locus coeruleus (LC), serotonin neurons in the raphe nuclei of the brainstem, and neurons of the olfactory system, cerebral hemispheres, spinal cord, and peripheral autonomic nervous system. This "nondopaminergic" pathology is likely responsible for the nonmotor clinical features. As PD progresses, the involvement of these systems exacerbates the Non-motor symptoms, which are increasingly recognized as key determinants of patient disability and quality of life. **(3)**

TABLE NO 1- SHOWING NON-MOTOR FEATURES OF PD

CLINICAL FEATURES	DS (4)	HS (5)	API (6)	GW (7)	KD (8)
OLFACTORY PROBLEMS					
HYPOSMIA	+	-	-	-	-
ANOSMIA	-	+	-	-	-
MOOD & COGNITIVE DISTURBANCES					

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COGNITIVE IMPAIRMENT	-	+	+	-	-
DEMENTIA	-	+	+	-	-
ANXIETY	+	-	+	-	-
DEPRESSION	+	+	+	+	
MELANCHOLIA	-	-	-	-	+
PARANOID FEARS	-	-	-	-	+
APATHY	+	-	-	-	-
HALLUCINATIONS	+	-	-	-	-
PSYCHOSIS	+	-	-	-	-
MENTAL DISTURBANCES	-	-	-	+	-
SLEEP RELATED PROBLEMS					
SLEEP DISTURBANCES	+	+	-	-	-
FRAGMENTED SLEEP	-	+	+	-	-
HYPERSOMNOLENCE	+	-		-	-
EXCESSIVE DAY TIME SLEEP	-	-	+	-	-
POOR DAY TIME FUNCTIONING	-	-	+	-	-
REM SLEEP BEHAVIOURAL DISTURBANCES	+	+	+	+	-
GENITAL DISTURBANCES					
ERECTILE FAILURE	+	-	-	-	-
LOSS OF LIBIDO	+	-	-	-	-
HYPER SEXUALITY	+	-	-	-	-
SEXUAL PROBLEM	+	+	-	-	+
AUTONOMIC DYSFUNCTIONS					
CONSTIPATION	+	-	+	+	+
SPINCTOR DISTURBANCE	+	-	-	-	-
NOCTURIA	-	-	+	-	-
URINARY INCONTINANCE	-	-	-	+	-
DIFFICULTY IN MICTURITION	-	-	-	-	+
FATIGUE	+	-	-	-	-
ORTHOSTATIC HYPOTENSION	-	+	+	-	-
DROOLING	+	-	-	-	-
WEIGHT LOSS	+	-	-	-	-
POSTURAL HYPERTENSION	-	-	-	+	-
SIALORRHEA	-	-	-	+	+
SEBORRHEA	-	-	-	-	+
SENSORY DISTURBANCES					
PAIN	+	+	+	+	-
UNDEFINED MUSCLE PAIN	-	-	+		-
ABDOMINAL DISCOMFORT	-	-	-	+	-
DYSESTHESIA IN FEET	-	-	-	+	-
PAINFUL NECK MOVEMENTS	-	-	-	+	-
COLD HANDS & FEET	-	-	-	+	-
VAGUE BODY PAINS	-	-	-	-	+
GASTROINTESTINAL DISTURBANCES					
GASTROPARESIS	-	+	-	-	-
MISCELLANEOUS					
DYSKINESIA	-	-	-	-	-
DYSPHAGIA	-	-	-	+	
DYSTONIA	-	-	-	+	-
PAROXYSMAL AKINESIA	-	-	-	-	+
SPEECH DIFFICULTY	-	-	-	-	+

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DIAGNOSIS OF PARKINSON'S DISEASE CAN BE DONE AS FOLLOWS:[9]

The diagnosis of Parkinson's disease (PD) is primarily clinical, based on a comprehensive evaluation of the patient's medical history, clinical features, and neurological examination.

1. DETAILED HISTORY TAKING

2. DIAGNOSTIC TESTS CLINICALLY:

A. TREMOR: - Usually resting tremor, pill rolling movements, diminishes with movements and attention

B. RIGIDITY: -Lead pipe (more in lower limbs and trunk), Cog wheel (more in upper limbs). Following are the tests for rigidity:

a) Positive Head drop test: When the patient is in supine position and relaxed, the examiner quickly lifts and drops with considerable force, but with parkinsonian rigidity, it drops slowly on each of the several attempts.

b) Imaginary pillow: - if the pillow is quickly pulled from under the head of a recumbent Parkinson's patient, rigidity keeps the head poised in the air.

C. BRADYKINESIA: - This refers to slowness of movement.

Following are the tests for Bradykinesia/ Akinesia: adopted by Carlie, Adams, Kulkarni, Shukla, Dhruve to assess the effect of therapy on Bradykinesia:

a) Picking of pins with hands:

b) Buttoning time-:

c)Marie sign:
Blinking per minute is counted.

d) Rapid Alternating movements:
- Repeatedly touching index finger with thumb
- Opening and closing of fists
- Pronation and supination of hands

e) Chest expansion:

f) Walking Time:

g) Facial bradykinesia:
- It is characterized by Decreased Facial Expression.
- Speech may become softer, less distinct, or more monotonal. In more advanced cases, speech is slurred, poorly articulated, and difficult to understand.

h) Truncal bradykinesia -It results in slowness or difficulty in rising from a chair, turning in bed, or walking.

i) Bradykinesia in lower and upper limbs: If walking is affected, patients may take **Smaller Steps** and **Gait Cadence** is reduced.

D. POSTURE: - Stooped posture / Flexed attitude. Postural instability is assessed by following tests:

a) Propulsion test-The combined rigidity and bradykinesia cause a characteristic posture stooped forward with a hip and knee flexed the step becoming quicker as a movement progresses "festination". There may be difficulty in stopping, a slight push from back may cause rapid forward movement 'propulsion' sudden change in direction cannot be made.

b) Retropulsion test- A slight push from front to the patients with Parkinson's disease will often take several steps

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backwards and be unable to maintain their stability.

E. GAIT: - Short stepped festinating gait/ Shuffling gait/ Parkinsonian gait - It is a type of gait (walking) characterized by a flexed trunk, legs flexed stiffly at the knees and hip. Takes initially progressively increased speed of steps and later takes multiple short and slow steps while walking. The center of gravity usually altered because the person cannot stay balanced. Turning and changing the directions are difficult. Patients with this gait also have difficulty stopping their gait after starting due to muscle hypertonicity.

F. GLABELLAR TAP SIGN/ (MYERSON'S SIGN): - It is usual to find it in Parkinson's disease and can be helpful in early diagnosis. Repeated tapping of the bridge or at the root of the nose is a accompanied by synchronous blinking. In the normal response blinking disappears after 4-5 taps.
G. BLEPHAROSPASM: - Spasmodic blinking or involuntary closing of the eye lids, a type of dystonia

H. MYOCLONUS: - Jerky involuntary movement of arms and legs, usually occurring during sleep

I. STELLA WAG SIGN: - Slight widening of palpebral fissure.

J. ROMBERGISM: - The patient sways from the heels, slightly when the yes are open, but very markedly when the eyes are closed, to the extent that he will either fall or separatwe his legs to achieve a broader base.

K. OLFACTORY TESTING: -

▪ It is a inexpensive, but useful supplementary exam and should be performed in each patient presenting with suspected Idiopathic PD. Commercial Kits are available, where different odorants, including trigeminal irritants and controls, are presented to the patient (eg. Sniffin sticks).

▪ It is a early clinical biomarker to differentiate PD from other atypical parkinsonian syndromes, as olfaction can also be impaired in patients with MSA, bit it seems mostly unaffected in PSP or CBD

L. MENTAL STATUS EXAMINATION

M. SCALES FOR DIAGNOSIS OF PARKINSON'S DISEASE

1.MDS-UPDRS SCALE
2. HOEHN AND YAHR SCALE
3. NMSS PD SCALE
4. PDQ 39 QUESTIONNAIRES

3.CLINICAL BIOMARKERS: As shown in the table 2 & 3

TABLE NO 2- SHOWING BIOCHEMICAL BIOMARKERS FOR DIAGNOSIS OF PD : [(10)]

SL NO	BIOCHEMICAL PARTICULARS	BIOMARKERS
1	**Mitochondrial Dysfunction and Oxidative stress Related Biomarkers**	Urate, Protein DJ-1, Coenzyme Q10, , Homocysteine(Hcy), Hydroxy deoxy guanosine (8-OhdG), Advanced Oxidised Protein Products (AOPP)
2	**Abnormal Protein accumulation and aggregation related biomarkers**	α-synuclein, Ubiquitin-C-Terminal Hydrolade-L(UCH-L-1), Beta-Glucocerebrosidase, Amyloid Beta 1-42 (Aβ42), Neurofilament Light Chain Protein (NFL)
3.	**Neurotrophins Related Biomarkers**	Brain-Derived Neurotrophic Factor (BDNF), Insulin-Like Growth Factor 1 (IGF-1),
4	**Neuroinflammatory Reaction Related Biomarkers**	Inflammatory cytokines such as - IL-2, IL-6, IL-10, TNF-α, IL-1β and IFN-γ

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5	**CSF Biomarkers**	Alpha synuclein, Glial fibrillary acidic protein (GFAP), Beta-amyloid 1-42, tau, p-tau, YKL-40
6	**Other Biomarkers**	MicroRNA (miRNA), Peptides

TABLE NO 3- Showing Genetic Biomarkers for Diagnosis of PD: [10]

SL NO	Conditions	Genetic Biomarkers
1	**Autosomal recessive (early onset)**	Parkin, Protein DJ-1, PINK 1
2	**Autosomal recessive (juvenile onset)**	ATP13A2, DNAJC6
3	**Autosomal dominant**	SNCA, LRRK2, VPS35
4	**Others**	GBA etc…

Note:
Up to now, no laboratory test is available for the diagnosis of idiopathic Parkinson's disease and no single marker has been identified so far. There is no routine workup, but assessment of Serum Copper, Urine Copper and Ceruloplasmin may be indicated especially in patients with young onset PD, if Wilson's disease is suspected. [9]

TREATMENT FOR NON- MOTOR FEATURES OF PARKINSON'S DISEASE:

At present there is no cure for PD. [11] The primary goal in the management of PD is to treat the symptomatic motor and Non-motor features of the disorder, with the objective of improving the patient's overall quality of life.[12]

TREATMENT OF PD CAN BE FURTHER CATEGORISED AS:

1. General Management
2. Pharmacological Management
3. Surgical Management
4. Non-Pharmacological Management
5. Current Management of PD under Investigations

1. GENERAL MANAGEMENT:[13] [14]

- It is important to encourage the patient to continue in his job and daily activities, since restriction of activity leads to rapid deterioration.
- In general, most specialists recommend initiating treatment when symptoms are impacting on everyday life, although some favour treatment as soon as the diagnosis is made.

2. PHARMALOGICAL MANAGEMENT: [15][16][17]

Pharmacotherapy is the mainstay of management. Drug treatment for PD remains symptomatic rather than curative, and there is no evidence that any of the currently available drugs are neuroprotective. The mainstay of antiparkinsonian therapy is dopamine replacement. This may be achieved either directly with levodopa or indirectly with dopamine agonists or other drugs that enhance dopaminergic transmission. The medical treatment of PD is challenging at every phase of the disease. The goal of therapy is to maximize the control of motor symptoms and minimize the complications of treatment which are also due to progression of the disease. Treatment is begun when patients experience functional or social disability because of their symptoms. The age of the patient, the most problematic symptom, severity of disability, presence of cognitive impairment, co-morbid medical conditions and cost of drugs influence the choice of drugs for early treatment.

TABLE NO 4- SHOWING PHARMACOLOGICAL TREATMENT FOR NON- MOTOR SYMPTOMS			
DRUGS	**AVERAGE DAILY DOSING**	**USES**	**SIDE EFFECTS**
DEPRESSION AND ANXIETY:			
a) Benzodiazepines:			
Alprazolam	1-4mg/day	Anxiety And Panic	Drowsiness, Dizziness, Depression, diarrhoea, Headache, Constipation

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Clonazepam	0.25mg/12hrs		Dizziness, Depression, Ataxia, Confusion, Dysarthria
Diazepam	2-10mg/12hr		Dizziness, diarrhoea, Rash, Ataxia, Somnolence
Lorazepam	1-4mg/day		
b) Selective Serotonin reuptake inhibitors:			
Fluoxetine	20mg/day	Depression, panic, anxiety	Nausea, Headache, Weakness, Insomnia, Diarrhoea
Sertraline	50mg/day		Nausea, diarrhoea, In somnolence, Dry-mouth, Dizziness
c) Serotonin/ Norepinephrine reuptake inhibitors (SNRI)			
Duloxetine	40-60mg/day	Depression and anxiety	Nausea, Dry-mouth, Somnolence, Headache, Fatigue
Desvenlafaxin	50mg/day		Nausea, Dry-mouth, Somnolence, Dizziness, Constipation
Milnacipran	12.5/day		Nausea, Headache, Constipation, Hot flush
Venlafaxine	75mg/day		Headache, Nausea, Insomnia, Asthenia, Dizziness
d) Tricyclic compounds:			
Amitrytilline	50-75mg/day	Depression and anxiety	Dry-mouth, Insomnia, Constipation, diarrhoea
Imipramine	75mg/day		Fatigue, Dry-mouth, Insomnia, Constipation, diarrhoea
Nortriptyline	150mg/day		Fatigue, Dry-mouth, Constipation, Headache, Insomnia
e) Additional Antianxiety:			
Buspirone	10-15mg/day	Generalised anxiety	Drowsiness, Nausea, Headache, diarrhoea, Insomnia
Propranolol	40mg/12hr	Panic attack/Anxiety	Depression, Fatigue, Insomnia, Nausea
Quetiapine	50mg/day	Depression/Anxiety	Dizziness, Fatigue, Dry-mouth, Headache, Constipation
Trazodone	150mg/day	Depression/Anxiety	Dizziness, Drowsiness, Headache, Fatigue
f) Other Antidepressants:			
Bupropion	100mg/12hrs	Depression	Headache, Nausea, Dry-mouth, Insomnia, Dizziness
Mirtazapine	15mg/day		Somnolence, Constipation, Dizziness, Confusion
EXCESSIVE DROOLING			
Atropine drops	-	Unwanted drooling	Confusion, Drowsiness, Hallucination,
Botulinum Toxin A Botulinum Toxin B	-		Urinary tract infection, Somnolence, Dizziness, Headache
Glycopyrrolate	8mg/day		Dry mouth, Dry skin, Constipation
Scopolamine patch	-		Dry-mouth, Drowsiness, Dizziness, Blurred vision
GASTROINTESTINAL PROBLEMS:			
a) Constipation:			
Lubipostine	24mcg/12hrs	Constipation	Nausea, diarrhoea, Headache, Vomiting
Polyethylene glycol	17g/day		Rashes, diarrhoea, Dehydration, Nausea

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b) Nausea and Vomiting;			
Ondansetron	4-16mg/day	Nausea and vomiting	Headache, Malaise, Constipation, Drowsiness, diarrhoea
Trimethobenzamide	30mg/day		Dizziness, Headache, Drowsiness
DEMENTIA			
Anticholinesterase inhibitors:			
Donapezil	**10mg/day**	Dementia	Nausea, diarrhoea, Insomnia, Headache
Galantamine	4mg/12hrs		Nausea, diarrhoea, Vomiting, Dizziness, Headache
Rivastigmine	1.5mg/12hrs		Nausea, diarrhoea, Vomiting, Dizziness, Headache,
PSYCHOSIS:			
Clozapine	12.5mg/day	Hallucinations/ Psychosis	Nausea, Somnolence, Insomnia, Constipation, Dizziness,
Pimavanserin	34mg/day	Hallucinations/ Delusions	Nausea, Hallucination, Constipation, Rash
Quetiapine	50mg/day	Hallucinations/ Psychosis	Dizziness, Fatigue, Dry-mouth, Headache, Constipation
SLEEPING DISORDERS:			
Amitriptyline	75mg/day	Insomnia	Insomnia, Dry mouth, Confusion, Dementia.
Clonazepam	0.25mg/12hr	REM Sleep Behavioural Disorder	Somnolence, Ataxia, Depression, Dizziness, Fatigue
Doxepin	25mg/day	Insomnia	Fatigue, Dry mouth, Constipation, Headache, insomnia
Eszopiclone	1mg/ day	Insomnia	Diarrhoea, Dizziness, Dry mouth, Dyspepsia,
Melatonin	3-5mg/day	Insomnia	Depression, Dizziness, Drowsiness, Headache
Mirtazapine	15mg/ day	Insomnia	Somnolence, Dizziness, weakness, Constipation
Trazadone	150mg/day	Insomnia	Drowsiness, Dizziness, Headache, Fatigue, Nausea
COGNITION AND DAY TIME SLEEPINESS:			
Methylphenidate	25mg/day	Unable to focus, overly sleepy during the day, fatigue.	Nausea, Decreased appetite, Headache, Insomnia,
Memantine	5mg/day	PD related Dementia	Dizzziness, Confusion, Headache, Constipation, Somnolence
Modafinil	200mg/day	Unable to focus, sleepy during the day.	Headache, Nausea, Decreased appetite, Dizziness
ORTHOSTATIC HYPOTENSION:			
Fludrocortisone	0.1mg/day	Neurogenic orthostatic hypotension	Insomnia, Neuritis, High blood pressure, Headache
Pyridostigmine	180-540mg/ day		Weakness, Loss of consciousness, Drowsiness
Droxidopa	100mg/day		Headache dizziness, Nausea
URINARY INCONTINENCE:			
a) Anticholinergics:			

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Darifenacin	7.5mg/day	Overactive bladder	Dry mouth, Constipation, Dizziness, Nausea
Oxybutynin	2.5-5mg/day	Overactive bladder/ Incontinence	Dry mouth, Constipation, Somnolence, Nausea
Solifenacin	5mg/day	Overactive bladder	Dry mouth, Constipation, Dizziness, Nausea, Depression
Tolterodine	2mg/day	Overactive bladder	Constipation, Dizziness, Drowsiness, Headache
b) Beta 3 agonists:			
Mirabegrons	25-50mg/day	Overactive bladder	Headache, Constipation, diarrhoea, Dry mouth, Fatigue
c) Alpha 1 A blockers			
Alfuzosin	10mg/day	Overactive bladder, BPH	Headache, Constipation, Dizziness, Dry mouth, Fatigue, Nausea
Silodosin	8mg/day		Diarrhoea, Headache, Insomnia, Dizziness
Tamsulosin	0.4mg/day		Headache, diarrhoea, Nausea Dizziness, Rash, Insomnia
Terazosin	1mg/day		Dizziness, Asthenia, Nausea, Somnolence, Fatigue, Headache
d) Serotonin norepinephrine reuptake inhibitors: (SNRI)			
Duloxetine	40-60mg/day	Urinary incontinence due to stress	Nausea, Dry-mouth, Headache, Somnolence, Fatigue
APATHY			
a) Acetylcholinesterase inhibitors:			
Rivastigmine	1.5mg/12hrs	Memory loss	Dizziness, diarrhoea, Nausea, Vomiting, Headache
b) Dopamine Agonists:			
Piribedil	150-250mg/day	Depression	Nausea, Vomiting, Dizziness, Drowsiness
IMPULSE CONTROL AND RELATED DISORDERS			
Opioid Antagonists Naltrexone	25-50mg/day	Opioid dependences	Dizziness, diarrhoea, Nausea, Vomiting, Headache, Insomnia
ERECTILE DYSFUNCTION			
Sildenafil	50mg/day	Sexual impotency	Headache, Flushing, Dyspepsia, Nausea, Rash
FATIGUE			
MAO-B Inhibitors Rasagiline	1mg/day	Used to reduce tremors& issue related to movements	Headache, Nausea, Constipation, Depression
PAIN			
Oxycodone-Naloxone Prolonged Release	10-20mg/12hrs	Pain reduction	Headache, Nausea, Constipation, Insomnia
Rotigotine	2mg/day	Stiffness, Tremors, Body balancing.	Dizziness, Somnolence, Fatigue, Insomnia

3. SURGICAL MANAGEMENT: [19]

The Surgical procedures currently employed are:
a) Thalamotomy
b) Pallidotomy- Unilateral and Bilateral
c) Deep Brain Stimulation

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d) Adrenal Medullary Foetal Tissue Transplantation
e) Continuous enteral infusion of levodopa (Duo dopa)

4. NON-PHARMACOLOGICAL TREATMENTS: [20]

a) Physiotherapy
b) Occupational Therapy
c) Speech Therapy
d) Gait Training
e) Freezing Management
f) Exercise Therapy
g) Diet
h) Phytotherapy

5. CURRENT MANAGEMENT OF PD UNDER INVESTIGATIONS [21]

a) Calcium Homeostasis
b) Brain Iron Deposits
c) Peripheral Insulin Resistance
d) Faecal Microbiota Transplantation
e) Neurotrophic Factor Supplementation
f) Stem Cells Transplantation

Despite advancements, significant gaps remain in treating non-motor features of Parkinson's disease (PD). These include underdiagnosis, limited understanding of symptoms, and a lack of holistic, patient-centred approaches. Treatments often target specific symptoms without addressing root causes or the disease's complexity. Medications can cause side effects, while many symptoms, like fatigue and apathy, remain resistant to treatment. There's insufficient focus on neuroprotection, emotional well-being, and lifestyle integration. Long-term care strategies and personalized treatments are often lacking, leaving many patients dissatisfied. These challenges highlight the need for complementary approaches, such as Ayurveda, to provide holistic, individualized care alongside modern advancements.

In recent years, *Ayurvedic* treatments have gained attention for their potential role in managing various aspects of PD, particularly Non-motor symptoms. Among the numerous formulations utilized in *Ayurveda*, *Mahakalyanaka Ghrita* stands out due to its diverse therapeutic properties. *Mahakalyanaka Ghrita*, a traditional *Ayurvedic* formulation, is believed to possess Neuroprotective, Anti-inflammatory, Antiparkinsonian and rejuvenating effects. Its use has been documented in various classical texts as a remedy for disorders affecting the nervous system, with promising results in treating conditions like PD. The conceptual framework surrounding *Mahakalyanaka Ghrita* suggests that it may help in balancing the *doshas* (body energies) and promoting overall mental and physical health. This review aims to explore the relevance and effectiveness of *Mahakalyanaka Ghrita* in managing the Non-motor features of Parkinson's disease. Understanding the potential of such treatments may lead to more integrative and holistic approaches to PD management, complementing conventional medical therapies.

TABLE NO 5- SHOWING INGREDIENTS WITH *RASA PANCHAKA* OF *MAHAKALYANAKA GHRITA* [22]

SL NO	DRUG NAME WITH BOTANICAL NAME & FAMILY NAME	*RASA*	*GUNA*	*VEERYA*	*VIPAKA*	*DOSHAGNATA* AND *KARMA*
1	*Swetha Sariva Hemidesmus Indicus Asclepedeceae*	*Tikta Madhura*	*Guru, Snigdha*	*Sheeta*	*Madhura*	*Tridosha hara, Sukravardhaka, Ruchikara, Balya, Deepana*
2	*Krishna sariva Ichnocarpus frutescens*	*Tikta Madhura*	*Guru, Snigdha*	*Sheeta*	*Madhura*	*Tridosha hara, Sukravardhaka, Ruchikara, Balya, Deepana*

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	Ascleped -eceae					
3	*Haridra Curcuma longa Zingiberaceae*	*Tikta Katu*	*Ruksha, Laghu*	*Ushna*	*Katu*	*Kapha pitta shamaka, sothahara, ruchikara,*
4	*Daruharidra Berberis aristata Berberidaceae*	*Tikta*	*Laghu, Ruksha*	*Ushna*	*Katu*	*Pitta Kapha shamaka, Netrya, asya rogahara, karna rogahara, yakruduttejjaka,*
5	*Salaparni Desmodium gangeticum Papilionaceae*	*Madhura Tikta*	*Guru, Snigdha*	*Sheeta Ushna*	*Madhura*	*Vata-pittashamaka, brimhana, rasaymana, sophahara, vrishya.*
6	*Prisniparni Uraria picta Papilionaceae*	*Madhura katu*	*Laghu sara*	*Ushna*	*Madhura*	*Tridosha shamaka Vrishya, dahashamaka,*
7	*Phalini/ Priyangu Callicarpa macrophylla Verbenaceae*	*Tikta, Kashaya Madhura*	*Guru, Ruksha*	*Sheeta*	*Katu*	*Kapha Pitta hara Mutravirajaniya, Purisha sangrahaniya*
8	*Nata/ Jatamamsi Nardostachys jatamansi Valerianaceae*	*Tikta, Kashaya Madhura*	*Laghu, Snigdha*	*Sheeta*	*Katu*	*Tridosha shamaka Medhya, Dahahara, Balya, Bhutaghni, Nidrajanaka*
9	*Brihati Solanum indicum Solanaceae*	*Katu, Tikta*	*Laghu, Ruksha, teekshna*	*Ushna*	*Katu*	*Kapha Vata Shamaka Hridya, Pachana, Ruchikara, Shoolahara, Agnivardhaka,*
10	*Kushta Saussurea lappa Asteraceae*	*Tikta, Katu, Madhura*	*Laghu, Ruksha, Tikshna*	*Ushna*	*Katu*	*Kapha Vata shamaka sukrala, Shothahara*
11	*Manjishta Rubia cordifolia Rubiaceae*	*Kashaya Tikta Madhura*	*Guru, Ruksha*	*Ushna*	*Katu*	*Pitta Kapha shamaka, sothahara, netrya, , yonirogahara,*
12	*Nagakesara Mesua ferrea Clusiaceae*	*Kashaya, Tikta*	*Ruksha Laghu*	*Ushna*	*Katu*	*Kapha Pitta shamaka Pachana, Hrillasaghna, Sophahara,*
13	*Dadima Punica granatum Punicaceae*	*Kashaya, Madhura, Amla*	*Laghu, Snigdha*	*Anushna*	*Madhura*	*Tridosha hara Dahahara, tarpana, sukrala, medhya, balya, hridya.*
14	*Vella/ vidanga Embelia ribes Myrsinceae*	*Katu, Kashaya*	*Laghu, Ruksha Tikshna*	*Ushna*	*Katu*	*Kapha Vata hara, deepana, shoolahara,adhmanah ara, vibandhahara, vishaghna, ruchya, rasayana.*
15	*Talisapatra*	*Katu*	*Snigdha Guru*	*Ushna*	*Madhura*	*Tridoshashamaka*

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	Abies webbiana Coniferae	*Tikta Madhura*				*Ruchikara, Deepana, Mukharogahara, Hridya.*
16	*Ela Elletaria cardomomum Zingiberaceae*	*Katu*	*Laghu, Ruksha*	*Ushna*	*Katu*	*Kapha Vata hara, hrillasanashaka, rochaka*
17	*Malathimukula Aganosma heynei Apocynaceae*	*Tikta, Kashaya*	*Laghu, Snigdha, Mrdu*	*Ushna*	*Katu*	*Tridosha hara*
18	*Utpala/Kumudha Nymphea stellata Nymphaceae*	*Madhura, kashaya, tikta*	*Laghu, snigdha, picchila*	*Sheeta*	*Madhura*	*Kapha Pitta , daha prashamana, shamaka*
19	*Danti Baliospermum montanum Euphorbiaceae*	*Katu*	*Guru, Tikshna*	*Ushna*	*Katu*	*Kapha Vata hara, Rechana, Deepana, Virechaka*
20	*Padmaka Prunus cerasoides Rosaceae*	*Kashaya, Tikta*	*Laghu, Snigdha*	*Sheeta*	*Katu*	*Kapha Pitta hara, vedanasthapana, vrsya*
21	*Hima/ chandana Santalum album santalaceae*	*Tikta, Madhura*	*Laghu, Ruksha*	*Sheeta*	*Katu*	*Pitta Kapha hara, Shramahara, Vrysya, Dahahara, Saumanasya Janana, Hridya, Angamarda Prashamana*
22	*Go ghrita*	-	-	-	-	-
23	*Go Ksheera*	*Madhura*	*Mridu, snigdha, bahala, slakshna, picchila, guru, manda, prasanna, Alpa abhishyanda (sushruta)*	*sheeta*	*Madhura*	*Vatapittahara Jeevaniya Rasayana, ojovardhana,*
24	*Vira/ Shatavari- Asparagus racemosus Liliaceae*	*Madhura, Tikta*	*Guru, Snigdha*	*Sheeta*	*Madhura*	*Vata-Pitta shamaka, Rasayana, medhya, pushti vardhaka, netrya, shukravardhaka, balya, shothahara, vrsya,*
25	*Meda Polygonatum verticillatum Liliaceae*	*Madhura*	*Guru*	*Sheeta*	*Madhura*	*Pitta- Vata hara, Vrishya, brihmana, shukrakrit*
26	*Mahameda Polygonatum cirrhifolum Liliaceae*	*Madhura*	*Guru*	*Sheeta*	*Madhura*	*Vata Pitta hara, Vrishya, shukravivardhana, ruchya.*

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27	*Kakoli Roscoea purpurea Zingiberaceae*	*Madhura*	*Guru, snigdha*	*Sheeta*	*Madhura*	*Vata Pitta hara, Sukrala, brihmana, jivana, vrishya*
28	*Kapikachu Mucuna pruriens Papilionaceae*	*Madhura, Tikta*	*Guru, Snigdha*	*Ushna*	*Madhura*	*Tridosha shamaka, Vrishya, brihmana, balya,*
29	*Vishani/ karkatashringi- Pistacia intergerrima Anacardaceae*	*Kashaya, Tikta*	*Laghu, Ruksha Guru*	*Ushna*	*Katu*	*Kapha Vata hara Rochaka*
30	*Mashaparni Teramnus labialis Fabaceae*	*Madhura, Tikta*	*Laghu, Snigdha*	*Sheeta*	*Madhura*	*Vata Pitta hara, Balya, Jivaniya, Shukrala,Pushtivardhana, Daha-jwarapaha*
31	*Mudgaparni Vigna trilobata Fabacae*	*Madhura*	*Laghu, Ruksha*	*Sheeta*	*Madhura*	*Tridosha hara, Chakshushya, Jeevaniya,Shukrala*

FIGURE NO 1- SHOWING PICTURES OF THE DRUGS OF *MAHAKALYANAKA GHRITA*

Hemidesmus indicus	***Uraria picta***
 	 
Ichnocarpus frutescens	***Callicarpa macrophylla***
 	 
Curcuma longa	***Nardostachys jatamansi***
 	 
Berberis aristata	***Solanum indicum***

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Desmodium gangeticum		***Saussurea lappa***	
			
Rubia cordifolia		***Elletaria cardomomum***	
			
Mesua ferrea		***Aganosma heynei***	
			
Punica granutum		***Nymphea stellata***	
			
Embelia ribes		***Baliospermum montanum***	

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Abies webbiana		***Prunus cerasoides***	
			
Santalum album		***Mucuna pruriens***	
			
Asparagus racemosus		***Pistacia intergerrima***	
			
Polygonatum verticillatum		***Teramnus labialis***	
			
Polygonatum cirrhifolium		***Vigna trilobata***	

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Roscoe purpurea		***Go ghritha and go ksheera***	
			

Table No-6- SHOWING ANALYTICAL REVIEW ON DRUGS OF *MAHAKALYANAKA GHRITA*

DRUGS	THERAPEUTIC ACTIONS
SWETHA SARIVA [23]	Anti-Inflammatory Activity, Antioxidant, Nootropic, Neuroprotective, Antinociceptive
KRISHNA SARIVA [24]	Anti Inflammatory, Antioxidant, Neuroprotective, Antinociceptive
HARIDRA [25]	Anti-inflammatory, Antioxidant, Neuroprotective, Immunomodulator, Anxiolytic, Nootropic, Antidepressant
DARUHARIDRA [26]	Anti-inflammatory, Antioxidant, Neuroprotective
SHALAPARNI [27]	Anti-inflammatory, Immunomodulatory, Aphrodisiac, Antinociceptive, Anxiolytic, Laxative
PRISHNIPARNI [28]	Anti-inflammatory, Antioxidant, Nervine Tonic, Analgesic, Aphrodisiac, Antinociceptive, Anxiolytic
PRIYANGU [29]	Anti-inflammatory, Antiarthritic, Antinociceptive, Antiarthritic
JATAMAMSI [30]	Antioxidant, Spasmolytic, Sedative, Useful in CNS Disorders, Antiparkinsonian, Neuroprotective, Anxiolytic
BRIHATI [31]	Anti-inflammatory, Antioxidant, Anticonvulsant, CNS Depressant, Laxative
KUSHTA [32]	Anti-inflammatory, Antioxidant, Analgesic, Carminative, Digestive, Aphrodisiac
MANJISHTA [33]	Anti-inflammatory, Antioxidant, Neuroprotective, Immunomodulator, Antiarthritic
NAGAKESHARA [34]	Anti-inflammatory, Antioxidant, CNS Depressant, Immunomodulator, Antinociceptive, Antiarthritic, Antidepressant
DADIMA [35]	Anti-inflammatory, Antioxidant, Neuroprotective
VIDANGA [36]	Antioxidant, Neuroprotective, Antinociceptive, CNS Depressant
TALISAPATRA [37]	Anti-inflammatory, Antioxidant, Anxiolytic, Antinociceptive, Anxiolytic
ELA [38]	Anti-inflammatory, Antioxidant, , Neuroprotective
MALATHI MUKULA [39]	Anti-inflammatory, Antioxidant,
UTPALA [40]	Anti-inflammatory, Antinociceptive
DANTI [41]	Anti-inflammatory, Antioxidant, Laxative
PADMAKA [42]	Antioxidant
SWETHA CHANDANA [43]	Anti-inflammatory, Antioxidant, Antidepressant
SHATAVARI [44]	Anti-inflammatory, Antioxidant, Immunomodulatory, Neuroprotective, Antinociceptive, Anxiolytic, Antidepressant
MEDA [45]	Anti-inflammatory, Antioxidant, Aphrodisiac, Anticonvulsant, Antinociceptive,
MAHAMEDA [46]	Anti-inflammatory, Antioxidant, Immune Enhancer, Aphrodisiac

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KAKOLI [47]	Anti-inflammatory, Immunostimulant, Antioxidant, Antiarthritic Immunomodulator, Nootropic, Antidepressant Antiparkinsonian
KAPIKACCHU [48]	Antiparkinsonian, Neuroprotective
KARKATASHRINGI [49]	Anti-inflammatory, Antioxidant, Anticonvulsant, Muscle Relaxant, Improved Digestion, Antinociceptive
MASHAPARNI [50]	Immunomodulator, Antioxidant,
MUDGAPARNI [51]	Anti-inflammatory, Antioxidant, Sedative, Nootropic

DISCUSSION

Mahakalyanaka ghrita mentioned in *Ashtanga Hridaya Uttaratantra*, in *Unmada rogadhikara*, is a Polyherbal combination which includes 31 ingredients such as *Sariva, Krishna Sariva, Haridra, Daruharidra, Shalaparni, Prishniparni, Priyangu, Jatamansi, Brihati, Kushta, Manjishta, Nagakeshara, Dadima, Vidanga, Talisapatra, Ela, Malathi Mukula, Utpala, Danti, Padmaka, Swetha Chandana, Go Ghrita, Go Ksheera, Shatavari, Meda, Mahameda, Kakoli, Kapikacchu, Karkatashringi, Mashaparni, Mudgaparni having Tridoshahara, Balya, Brimhana, Sannipatagna, Rasayana, Pushtikara, Ayushya*, have *phalashruthi* as useful in *Moha, Upahata Chetas, Smritikaama, Amedhasi, Alpapavaka, Skalatvachi, Shosha, Apasmara.* One of the main drug present in *Mahakalyanaka ghrita* is ***KAPIKACCHU*** (Mucuna Pruriens) which is a natural source of L-dopa.

BASED ON *RASA*: Among 31 ingredients : 5 drugs have *Madhura rasa*, 4 drugs have *Madhura, tikta rasa*, 3 drugs have *kashaya, tikta rasa*, 3 drugs have *Tikta madhura rasa*, 2 drugs have *Katu rasa*, 1 drug have *Tikta katu* rasa, 1 drug have *Tikta rasa*, 1 drug have *Madhura, katu rasa*, 1 drug have *Katu, Tikta rasa*, 1 drug have *Tikta, katu, madhura rasa*, 1 drug have *Tikta, katu, madhura rasa*, 1 drug have *Kashaya, Tikta, madhura rasa*, 1 drug have *katu, Tikta, madhura rasa*, 1 drug have *Tikta, Kashaya rasa*, 1 drug have *Madhura, Kashaya, Tikta rasa*. Here drugs having *Madhura Rasa* decreases *Vata dosha*, drugs having *Madhura,Tikta, kashaya* rasa decreasing Pitta Dosha, drugs having *Tikta, katu, kashaya* rasa decreases Kapha Dosha, hence it shows it acts as *tridoshahara* and would have helped in reducing the symptoms of Non motor features of Parkinson's disease.

BASED ON *GUNAS*: Among 31 ingredients, 13 drugs have *Guru guna*, 13 drugs have *snigdha guna* which reduces *Vata* and *Pitta dosha*, 17 drugs have *Laghu guna*, 13 drugs have *ruksha guna*, 4 drugs have *Teekshna guna* which reduces *Kapha dosha*. Hence overall acts as *tridoshahara* and would have helped in reducing Non motor symptoms of Parkinson's disease.

BASED ON *VIRYA*: Among 31 ingredients, 16 drugs have *Ushna Virya* which reduces *Vata* and *kapha dosha* and 14 drugs have *Sheeta Virya* reduces *Pitta dosha*. Hence overall acts as *tridoshahara* and would have helped in reducing Non motor symptoms of Parkinson's disease.

BASED ON *VIPAKA*: Among 31 ingredients, 15 drugs have *Madhura Vipaka* reduces *Vata* and *Pitta doshas* and 15 drugs have *Katu Vipaka.* Hence overall acts as *tridoshahara* and would have helped in reducing Non motor symptoms of Parkinson's disease.

BASED ON *DOSHAGNATA*: Among 31 ingredients, 9 drugs have *Tridoshahara*, 7 drugs have *Vata-Pittahara*, 5 drugs have *Kapha-Pittahara*, 5 drugs have *Kapha- Vatahara*, 3 drugs have *Pitta-Kaphahara*, 1 drug have *Pitta-Vatahara*, 1 drug have *Vatahara*. Hence overall acts as *tridoshahara* and would have helped in reducing Non motor symptoms of Parkinson's disease.

BASED ON *KARMA*: Among 31 ingredients, *Swetha Sariva,Krishna Sariva, Jatamamsi, Shatavari, Meda, Kapikacchu, Mashaparni is Balya, Shalparni, kakoli, kapikacchu is Brimhana, Shalaparni, Vidanga, Shatavari, Goksheera* acts as *Rasayana, Brihati, Vidanga* is having *shoolahara karma, Padmaka* is *Vedanasthapaka, Chandana* is *Angamardhaprashamaka* and *Soumanasya janaka, Dadima* and *Shatavari* is *Medhya, Vidanga* and *danti* is *Vibandhahara* and *Virechaka r*espectively. *Kakoli, Mashaparni, Mudgaparni is Jeevaniya, Nagakeshara and Ela is Hrillasanashaka. Sariva, Brihati, Vidanga, Danti* is Used For *Deepana. Sariva, Brihati, Haridra, Vidanga,Talisapatra, Ela, Danti, Mahameda, Karkatashringi is Ruchikara. Brihati is Pachaka. Shalaparni, Prishniparni, Kakoli, Kapikacchu, Shatavari, Dadima, Sariva, Padmaka has Shukravardhaka* And *Vrishya Karma.* These would have helped in reducing Non motor symptoms of Parkinson's disease.

Most of the drugs in *Mahakalyanaka Ghrita* have properties such as Antioxidant, Anti inflammatory, Anxiolytic, Antidepressant, Immunomodulator, Nootropic, Antinociceptive, Antiparkinsonian which helps in managing Non Motor Features of Parkinson's Disease.

ANTIPARKINSON'S PROPERTY MODE OF ACTION IN PD: L-Dopa (Levodopa), Kaempferol and Quercetin of *Kapikacchu*[52] , Nardosinone of *Jatamamsi*[53]and Withaferin A of *Ashwagandha*[54] present in *Mahakalyanaka ghrita* has Antiparkinsonian effect, that might have helped in inhibiting the enzyme catechol-O-methyltransferase(COMT), potentiating dopamine activity and increasing the duration of action of levodopa and relieves signs and symptoms of Parkinson's disease. [55]

ANTIOXIDANT PROPERTY MODE OF ACTION IN PD: Oxidative stress is a key factor in the development of Parkinson's disease and plays an important role in the degeneration of dopaminergic neurons. Disruptions in the physiologic maintenance of the redox potential in neurons interfere with several biological processes, ultimately leading to cell death. However, oxidative stress is intimately linked to other components of the degenerative process such as mitochondrial dysfunction, excitotoxicity, nitric oxide toxicity and inflammation. [56] .Quercetin of *Shweta sariva* [57], Curcumin of *Haridra*[58], Solasodine of *Bruhati* [59], Kaempferol of *Kapikacchu,* Gallic acid of *Mahameda,* somniferine and withanine of *Ashwagandha,* Nardosinone of *Jatamamsi,* Berberine of *Daruharidra,* Alizarin of *Manjishta,* Calotropine of *Kushta,* of *Dadima,* Baliospermine of *Danti,* Fritillarin of *Kakoli,* Embelamine of *Vidanga,* Rutin of *Ela,* Quercetin of *Nagakeshara* and Alpha-santalol of *shwetachandana* exhibit Antioxidants property in *Mahakalyanaka ghrita* which may help to prevent the progression of Parkinson's disease by reducing the oxidative stress by neutralizing the free radicals. while preclinical studies have shown that antioxidants can maintain neuronal survival and activity in PD models.

ANTIINFLAMMATORY PROPERTY MODE OF ACTION IN PD: Inflammation is one of the components of degenerative process. Here, Berberine of *Daruharidra*,[60] Frutescine of *krishna sariva*,[61] Kaempferol of *Kapikacchu*[62],Oleanolic acid of *Priyangu*[63] Alpha-santalol of *shwetachandana,* Calotropine of *Kushta,* , Baliospermine of *Danti,* Embelamine of *Vidanga,* Rutin of *Ela,* Anti-inflammatory Withaferin A of *Ashwagandha,* Nardosinone of *Jatamamsi,* Quercetin of *Talisapatra,* Apigenin of *Krishna Sariva* present in *Mahakalyanaka ghrita* may help with PD by reducing inflammation in the brain and also slow or stop the progression of the disease by reducing damage to dopamine-replacing cells. [64]

NEUROPROTECTIVE PROPERTY MODE OF ACTION IN PD: Parkinson's disease is a chronic, progressive, neurodegenerative disease, hence neuroprotection is a pharmacological intervention plays important role in managing PD. Neuroprotective drugs present in L-Dopa (Levodopa), Kaempferol and quercetin of *Kapikacchu*[52] , Nardosinone of *Jatamamsi*[53], Curcumin of *Haridra*[58], Berberine of *Daruharidra*[60]**,** Punicalagins of *Dadima*[65], Shatavarin of *Shatavari*[66], Rutin of *Ela,* present in *Mahakalyanaka ghrita* helps in slowing the natural progression of the PD or prevents the loss of dopaminergic neurons in the substantia nigra, also helps in reducing oxidative stress, mitochondrial dysfunction, protein aggregation, inflammation, excitotoxicity, cell death, iron accumulation, and helps in stimulating neurotrophic factors. [67]

IMMUNOMODULATORY DRUGS MODE OF ACTION IN PD: Researchers identify an immunomodulatory drug as a potential treatment for Parkinson's disease. Astrocytes in the brain of Parkinson's patients over express the inflammatory cytokine IL-6, which induces the death of dopaminergic neurons. Hence Curcumin of *Haridra*[58]**,** Withaferin A of *Ashwagandha*[54], Shatavarin of *Shatavari*[66], Baliospermine of *Danti*[68],β-sitosterol of *Shalaparni* [69] are having immunomodulatory property in *Mahakalyanaka ghrita* helps in blocking the effect of IL-6 secreting astrocytes and prevents nerve cell death in PD. [70]

ANXIOLYTIC PROPERTY MODE OF ACTION IN PD: Anxiety disturbances is the most common non motor symptom in PD which might be due to neurochemical degeneration of subcortical nuclei and ascending dopamine, norepinephrine, and serotonin(5-HT) pathways within the basal ganglia- frontal circuits. Anti- anxiety drugs like Nardosinone of *Jatamamsi*[53], Curcumin of *Haridra*[58]**,** Quercetin of *Talisapatra*[71], β-sitosterol of *Shalaparni* [69], Kaempferol of *Prishniparni*[72] ,in PD helps in correcting the above pathology, thereby reducing the symptom. [73]

ANTIDEPRESSANT PROPERTY MODE OF ACTION IN PD: Antidepressants like Curcumin of *Haridra*[74] , Shatavarin of *Shatavari*[66], Withaferin A of *Ashwagandha*[75], Quercetin of *Nagakeshara* [76]helps in stimulating the dopaminergic, serotonergic and non-adrenergic neurotransmitter systems and increases serotonin concentration in the synaptic cleft by inhibiting serotonin reuptake by the presynaptic membrane and hence reduces depression. [77]

ANTINOCICEPTIVE PROPERTY MODE OF ACTION IN PD: Pain is one of the common non motor feature in PD. Antinociceptive drugs like Hemidesmine of *Sariva*[78] β-sitosterol of *Meda*[79], Desmodine of *Shalaparni* [80]present in

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Mahakalyanaka ghrita acts on dopaminergic system might be involved in pain modulation, probably through various cortical connections to the basal ganglion, including the limbic system and the sensory cortex and helps in reducing pain in PD. [(81)]

NOOTROPIC PROPERTY MODE OF ACTION IN PD: Drugs like Curcumin of *Haridra*[(82)], Nardosinone of *Jatamamsi*[(83)], Withaferin A of *Ashwagandha*[(84)], Quercetin of *Nagakeshara*[(85)] ,having Nootropic property affects the brain performances through number of mechanisms or pathways such as dopaminergic pathways and helps in enhancing cognitive performance and mental function such as memory, creativity, motivation and attention. Previous researchers have reported the influence of nootropics on treating memory disorders such as Parkinson's disease, Alzheimer'sdisease etc. [(86)]

MODE OF ACTION OF *GO-GHRITA* W.R.T. NEUROPROTECTION

Butyrate, present in cow ghee, is able to cross the "blood-brain barrier" and exert neuroprotective effects. Once in the brain, butyrate can enhance the expression of "brain-derived neurotrophic factor (BDNF)", a protein that supports the survival and growth of neurons, including dopaminergic neurons that are affected in Parkinson's disease. Butyrate also helps in regulating histone deacetylases (HDACs), which are enzymes that control gene expression related to inflammation and cell survival. By inhibiting HDACs, butyrate promotes "Anti-apoptotic" pathways (prevents cell death) and enhances neuronal survival, making it a potential neuroprotective agent for PD. [(87)]

CONCLUSION

Mahakalyanaka Ghrita offers a promising avenue for addressing the often-overlooked non-motor features of Parkinson's disease. With its multifaceted therapeutic potential rooted in *Ayurvedic* wisdom, it harmonizes neuroprotective, cognitive-enhancing, and mood-stabilizing properties in a single formulation. As science increasingly acknowledges the interplay of mind and body in neurodegenerative disorders, this ancient preparation may bridge the gap between tradition and modernity, providing holistic relief to patients. By integrating *Mahakalyanaka Ghrita* into contemporary research and clinical practice, we can unlock its full potential, nurturing not just the nervous system but the essence of life itself by bringing a paradigm shift in Parkinson's care.

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