KAPIKACCHU

CLINICAL RETROSPECTIVE AND *DROSOPHILA* STUDIES

A THESIS SUBMITTED TO

THE UNIVERSITY OF TRANS-DISCIPLINARY HEALTH SCIENCES AND TECHNOLOGY

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BY

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THE UNIVERSITY OF TRANS-DISCIPLINARY HEALTH SCIENCES AND TECHNOLOGY
Private University Established in Karnataka by ACT 35 of 2013

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DECLARATION BY THE CANDIDATE

I declare that this thesis "*KAPIKACCHU*- CLINICAL RETROSPECTIVE AND *DROSOPHILA* STUDIES" submitted for the award of Master of Science to THE UNIVERSITY OF TRANS-DISCIPLINARY HEALTH SCIENCES AND TECHNOLOGY, Bengaluru, is my original work, conducted under the supervision of Dr. Megha and co-supervision of Dr. Prasan Shankar. I confirm that no part of the work reported herein has been submitted for a degree or examination at any other university. References, funding and material obtained from other sources have been duly acknowledged, and no part of this dissertation has been plagiarised.

Place: Banglore

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Date:19 June 2024

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THE UNIVERSITY OF TRANS-DISCIPLINARY HEALTH SCIENCES AND TECHNOLOGY

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CERTIFICATE FROM THESIS SUPERVISOR/S

This is to certify that the work incorporated in this thesis **"*KAPIKACCHU* - CLINICAL RETROSPECTIVE AND *DROSOPHILA* STUDIES"** submitted by Dr. Renuka A was carried out under my/our supervision. No part of this thesis has been submitted for a degree or examination at any other university. References, help and material obtained from other sources have been duly acknowledged. I confirm the originality of the work and that there is no plagiarism in any part of the thesis.

Dr Megha Associate proffesor, TDU	Guide	 19 JUNE 2024
Dr. Prasan shankar IAIM Healthcare Centre, Banglore	Co-Guide	 19 JUNE 2024

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SUMMARY

Kapikacchu (*Mucuna pruriens*) is a significant herb in traditional Indian medicine. For centuries, it has been integral to Ayurvedic practices, prized for its strengthening (*Balya*), nourishing (*Brumhana*), and aphrodisiac (*Vajikara*) properties. It has gained attention for its potential in treating Parkinson's disease (PD), the second most common neurodegenerative disorder. This is due to high L-DOPA content – a precursor of dopamine.

In this study, we aim to provide a review of the pharmaceutical property of *Kapikacchu, as* mentioned in classical texts, we conduct a detailed review of Ayurvedic texts and modern research to gather comprehensive information on *Kapikacchu*'s properties. This helps bridge traditional knowledge with contemporary science.

The second part of the study investigates the effects of *Kapikacchu* using fruit flies (*Drosophila melanogaster)* as a model organism. By utilising both wild type (*CS*) and Parkinson's mutant flies, we aim to understand the herb's metabolic impacts and validate its traditional uses scientifically.

We also analyze prescription patterns at the IAIM Healthcare Center to understand how Ayurvedic doctors use *Kapikacchu* in practice, including common dosages and treatment contexts.

Overall, this research connects ancient Ayurvedic wisdom with modern science to substantiate the health benefits of *Kapikacchu* and enhance its use in treating Parkinson's disease.

PERSONAL REFLECTION

Working on this dissertation has greatly influenced my personal growth. It taught me the importance of planning, patience, and careful work in both science and everyday life. Getting ethical clearance and dealing with hospital processes were challenging but valuable experiences, showing me the need to follow rules carefully. Adjusting to the wet lab work, with its long hours and new tasks like taking care of fruit flies and setting up experiments, was initially tough. However, facing these challenges helped me overcome my fears and become more focused, ultimately finding joy in the work. This experience improved my time management skills, helping me prioritize tasks and set goals better. Participating in lab meetings and learning new skills expanded my knowledge and critical thinking, sparking a passion for science. This journey has deepened my love for research and motivated me to pursue a career in it, aiming to make a positive impact on society.

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LIST OF ABBREVIATIONS

MP- *Mucuna Pruriens*

PD- Parkinson's disease

ELS- Early life starved

AEL- After egg laying

API- Ayurvedic Pharmacopoeia of India

EMR- Electronic medical record

L-DOPA- Levodopa

HMIS- Health Management Information System

MR number- Medical record number

MS Excel- Microsoft Excel

I-AIM- Institute of Ayurveda and Integrative Medicine

ND - Normal corn diet

CS – *Canton-S*

1.INTRODUCTION

1.1 *Kapikacchu* (*Mucuna pruriens (L.) DC*)

Kapikacchu referred to as MP hereafter commonly known as velvet bean, is a significant and widely utilized herb in traditional and Indian medicine belonging to family Fabaceae. It is found extensively across tropical and subtropical regions worldwide. Renowned for its medicinal properties, *Kapikachhu* has been a cornerstone in traditional practices and Indian medical systems for a long time.

1.2 Vernacular names

Table 1.1 – Vernacular names (Bihari Dora, 2017)

Language	**Vernacular names**
Hindi	Konch, Kevanch
Kannada	Nasugunni
Malayalam	Naikkuran
Tamil	Poonaikaali
Bengali	Aalkushee, Alkusa
Telugu	Piliyadugu, Pilleeadugu
Gujrati	Kaucha, Kavach
Marathi	Khajkuhilee
Oriya	Baikhujnee
Punjabi	Aalkushee, Kavanch

1.3 Ecology and Botany

Mucuna pruriens (MP), a sturdy annual climbing legume native to southern China and eastern India, was historically a widely cultivated vegetable crop. Its cultivation spans Asia, America, Africa, and the Pacific Islands, where its pods are valued as a favored addition to human diets (Lampariello et al., 2012). In the Indian subcontinent, this legume is widely distributed in dry evergreen low forests and across the plains, appearing as bushes and hedges. In India, it is particularly recognized for its medicinal properties and is cultivated in regions such as Madhya Pradesh, Uttar Pradesh, and the Andaman and Nicobar islands.

a

b

c

Figure 1.1- a) Fresh pods, b)Mature dried pods, c) Flowers of *Mucuna pruriens* (Murthy & Nirawane, 2016)

Islands. It naturally thrives throughout the tropical plains of India, extending from the lower Himalayan range (Pathania et al., 2020). When the plant is young, it's densely covered with fuzzy hairs, but as it matures, it becomes mostly smooth, with few to no hairs. The leaves are trifoliate, alternate or spiraled, with gray-silky undersides and long, silky petioles. Leaflets are membranous, with smaller terminal leaflets and unequally sized lateral ones. The flowers, which can be dark purple, white, or lavender, are larger than typical pea flowers and appear in drooping racemes. The curved, longitudinal pods contain 4 to 6 seeds and are densely covered with persistent pale-brown or gray trichomes, which can cause

irritating blisters on contact with skin. The plant's length is about 15 m, with 2–3 mm long leaflets and flower heads measuring 15–32 mm, featuring 2–3 flowers in white and purple hues (Kavitha & Thangamani, 2014).

1.4 Taxonomic characteristics;

Kingdom -Plantae

Subkingdom -Tracheobionta

Superdivision -Spermatophyta

Division -Magnoliophyta

Class -Magnoliopsida

Subclass -Rosidae

Order -Fabales

Family -Fabaceae Lindl.

Genus -Mucuna Adans.

Species -*Mucuna pruriens (L.) DC.*

1.5 Phytochemistry

This leguminous plant is rich in bioactive compounds such as L-DOPA, alkaloids, flavonoids, and saponins, which contribute to its pharmacological effects. The chemical compounds found on seeds are mentioned on the Table 1.2 (L & S, 2007).

PHYTOCHEMICALS – *MUCUNA PRURIENS*		
5-HYDROXYTRYPTAMINE	GLUTAMIC-ACID	OLEIC-ACID
5-METHOXY-N,N-DIMETHYLTRYPTAMINE-N-OXIDE	GLUTATHIONE	PALMITIC-ACID
5-OXYINDOLE-3-ALKYLAMINE	GLYCINE	PALMITOLEIC-ACID
ALANINE	HISTIDINE	PHENYALANINE

ARACHIDIC-ACID	INDOLE-3-ALKYLAMINE	PHOSPHORUS
ARGININE	IRON	PROLINE
ASH	ISOLEUCINE	PROTEIN
ASPARTIC-ACID	KILOCALORIES	PRURIENIDINE
BEHENIC-ACID	LECITHIN	PRURIENINE
BETA-CARBOLINE	LEUCINE	RIBOFLAVIN
BETA-SITOSTEROL	LINOLEIC-ACID	SAPONINS
BUFOTENINE	LINOLENIC-ACID	SERINE
CALCIUM	LYSINE	SEROTONIN
CARBOHYDRATES	METHIONINE	STEARIC-ACID
CHOLINE	MUCUNADINE	THIAMIN
CIS-12,13-EPOXYOCTADEC-TRANS-9-CIS-ACID	MUCUNAIN	THREONINE
CIS-12,13-EPOXYOCTADEC-TRANS-9-ENOIC-ACID	MUCUNINE	TRYPTAMINE
CYSTINE	MYRISTIC-ACID	TYROSINE
DOPA	N,N-DIMETHYLTRYPTAMINE	VALINE
FAT	N,N-DIMETHYLTRYPTAMINE-N-OXIDE	VERNOLIC-ACID
FIBER	NIACIN	WATER
GALLIC-ACID	NICOTINE	

Table 1.2 – Phytochemicals present in *Mucuna pruriens*.

Recently, three new lipid derivatives were identified from the n-hexane extract of *Mucuna pruriens* seeds: (Z)-Triactont-5,7,9-triene, (Z)-Docos-2,4,6-trien-1,8-diol, and (Z)-Docos-5-en-1-oic acid (L & S, 2007).

1.6 Nutritional and medicinal uses

Different parts of the *Mucuna pruriens* plant exhibit medicinal properties (L & S, 2007). *Mucuna pruriens* is considered a valuable source of dietary proteins due to its high protein content (23–35%) and digestibility (Lampariello et al., 2012). Traditionally, the velvet bean has been used as a food source by various ethnic groups in several countries. It is cultivated across Asia, America, Africa, and the Pacific Islands, where its pods are consumed as vegetables and its young leaves serve as animal fodder. In India, the mature seeds are traditionally consumed by the Kanikkar tribe of South India after being repeatedly boiled (Lampariello et al., 2012).

A review by Pathania et al., underscore the therapeutic potentials of MP, spanning from its efficacy against snake poisoning to antimicrobial, anti-epileptic, neuroprotective, aphrodisiac, and antioxidant activities (Pathania et al., 2020). Contemporary medical practices have studied the utilisation of Mucuna seed preparations in Parkinson's disease (PD) management, given their natural source of L-Dopa (Levodopa) (Duke, 1981; Hernández-Orihuela et al., 2022; Manyam et al., 2004; Pathania et al., 2020; Rai et al., 2020; Rane et al., 2019; Rima et al., 2023; Sharma et al., 2016).

1.7 Levodopa and neuroprotective effect

Studies have identified antioxidant and mitochondrial energy-enhancing compounds, such as coenzyme Q-10 and NADH, in *Mucuna pruriens* (Manyam et al., 2004). Additionally, it contains L-DOPA, a precursor to dopamine, which is commonly used in the treatment of Parkinson's disease. Some studies suggest that the plant's effectiveness in managing neurodegeneration may be attributed to its antioxidant properties in conjunction with L-DOPA (Manyam et al., 2004; Rai et al., 2020). L-DOPA was first isolated from the seeds of *Mucuna pruriens* (MP) in 1937 (Rai et al., 2020). Once the value of L-DOPA in treating Parkinson's Disease (PD) was recognized, scientific interest in L-DOPA-rich plants surged. Three open-label studies (HP-200 in Parkinson’s Disease Study Group, 1995; Nagashayana et al., 2000; Vaidya et al., 1978) involving 18 to 60 patients each, administered an average dosage of 45 g/day of Mucuna seed powder

extract (containing approximately 1500 mg of L-DOPA). These studies reported significant improvements in PD symptoms within 12 to 20 weeks (Rai et al., 2020).

1.8 Specific use in PD

Studies have shown that Mucuna seed powder exhibits better efficacy in PD, leading to a significantly faster onset of effect, longer duration of action, and higher peak L-dopa plasma concentrations compared to standard L-dopa/carbidopa treatment (Cilia et al., 2017; Kavitha & Thangamani, 2014). While L-dopa in *Mucuna pruriens* contributes to its effectiveness, studies suggest it also benefits PD patients through additional mechanisms. Studies found significantly improved behavioural deficits in PD models through mechanisms beyond just L-dopa content. It uniquely affects basal ganglia electrophysiology, confirming that its anti-PD effects are not solely due to natural L-dopa but also due to its combination of multiple constituents (Lieu et al., 2012).

1.9 *Kapikacchu* (*Mucuna pruriens)* – In Ayurveda literature

In the annals of Ayurveda, *Kapikacchu* finds mention dating back to the samhitha period (1500 BCE – Seventh century), where it is documented as a remedy for *vajikarana chikitsa (*Aphrodisiac*), vatavyadhis* (diseases caused due to the vitiation of vata), and various other conditions related with raktha (~blood), often as an integral component of distinct formulations (Table 1.3).

Table 1.3- Formulations using Kapikacchu (Mishra & Tiwari, 2021)

Sl.no	Formulation
1.	Bramha rasayana
2.	Agastya Rasayana (Hareetaki Rasayana)
3.	SwadamstradiGhrita
4.	Saradi Ghrita
5.	Amrita prasa ghrita
6.	Svadamshtradi Ghrita
7.	Vidaryadi Ghrita
8.	Mashadi Kashaya
9.	Svayam guptadi churna

10.	Gokshuraadi Churna
11.	Satavaryadi churna
12.	Vanari gutika
13.	Kameswara Modaka
14.	Kapikachu paka
15.	Svayam gupta Ikshuraka Yoga
16.	Brhatmasa Taila
17.	Amrita Taila

Kapikacchu is a renowned *Vrishya* (spermatogenetic) drug referenced in Ayurvedic texts dating back to the Caraka and Sushruta samhitas. It is also used as a balya (promoting muscle mass and body weight) and is recommended for vajikarana chikitsa (aphrodisiac therapy). Every part of the plant holds medicinal value, with the seeds and roots being particularly significant for their ability to provide vital energy (Mishra & Tiwari, 2021). A drug review on *Kapikacchu*, report that *Kapikacchu* is not mentioned in Vedic literature, and the term is not commonly used even in Brihattrayi (Mishra & Tiwari, 2021). In the three Samhitas (Caraka, Sushruta, and Vagbhata), this plant is primarily referred to as Atmagupta, Svayamgupta, and Markati. Ayurveda physicians use *Mucuna pruriens* as a medicine to treat *Kampa vata* (~Parkinson's disease), *Klaibya* (~libido) and various other disorders caused due to the vitiation of *vata dosha*.

1.10 Introduction to *Kampa vata*;

The term "Kampavata" is formed by combining two words: "कम्प," derived from the root "कपि" and suffixed by "घन्," which signifies movement or shaking or tremors. "वात," derived from the root "वा" and suffixed by "क्थ," pertains to the functions described in the Nirukti as "Gati" (movement) and "Gandhan" (perception). Therefore, "Kampavata" denotes a disorder of Vata where there is an imbalance without the equilibrium of the three doshas and is characterized by tremors (Kampa) (Kuldeep & Prashanth, 2019). Basavrajiyam provided a detailed description of Kampavata, whereas Acharya Madhavakara in Madhava Nidana was the first to use the term Kampavata, though he described it under the clinical condition Vepathu- characterised it by Sarvanga Kampa (tremors throughout the body) and Shiro Kampa (tremors in the head). Other Acharyas also used Vepathu

instead of Kampavata, and Vepathu being explained as one among eighty types of Nanatmaja Vatavyadhi (disease caused due to the vitiation of vata). Charaka and Sushruta mentioned symptoms like Kampa (tremors), Stambha (rigidity), Chestanasha (loss of vocal control), and Vakvikriti (speech disturbances) in various clinical contexts but did not categorize them as a distinct clinical condition. They used the term Vepathu, which resembles Kampavata, to discuss similar conditions. In Madhavanidan and Basavrajiyam, the Acharyas did not specify separate nidana (causes) for Kampavata. Instead, they regarded the general causes of Vatavyadhi as applicable to Kampavata as well.

Types - Although Madhavakara did not explicitly categorize the types of Kampavata, his descriptions of the symptoms suggest two types: Sarvanga Kampa (whole body tremors) and Ekanga Kampa (localized tremors) (Kuldeep & Prashanth, 2019; Madhavakara, 1997). Later, Basavarajiyam further clarified the types of Kampavata, identifying Sarvanga Kampavata (tremors all over the body) and Bahu Kampavata (tremors in the arms) (Nilakantha kotturu, 2008).

1.11 Parkinson's disease

Parkinson's disease (PD) is the second most common neurodegenerative disorder, second to Alzheimer's disease (AD). PD is characterized by progressive loss of dopaminergic neurons within the nigrostriatal as well as the formation of proteinaceous inclusions of alpha-synuclein (α-syn), i.e., Lewy Bodies (LBs). Parkinson's disease was first described by James Parkinson in 1817 in his work "An Essay on the Shaking Palsy" (Parkinson, 2002). Parkinson meticulously detailed the symptoms of what he referred to as "paralysis agitans," highlighting the hallmark features of the disease: tremors at rest, muscle rigidity, bradykinesia (slowness of movement), and postural instability (Goetz, 2011).

In the late 19th and early 20th centuries, further advancements were made in understanding PD. Jean-Martin Charcot, a French neurologist, expanded on Parkinson's initial findings, distinguishing PD from other neurological disorders and emphasizing the disease's unique clinical features (Goetz, 2011). The term "Parkinson's disease" was subsequently adopted in his honour.

The mid-20th century marked significant progress in the pathophysiology and treatment of PD. Arvid Carlsson's discovery of dopamine's role in the brain and the subsequent development of levodopa (L-DOPA) therapy revolutionized PD treatment (Carlsson, 1959). Carlsson's work, which earned him the Nobel Prize in 2000, demonstrated that dopamine deficiency in the basal ganglia is a key factor in PD pathology (Yeragani et al., 2010).

Continued research has since focused on genetic and environmental factors contributing to PD, as well as advancements in therapeutic approaches, including deep brain stimulation and neuroprotective strategies (Dauer & Przedborski, 2003). Today, PD remains an active area of research, with ongoing studies aimed at improving understanding, treatment, and ultimately, finding a cure (Lang & Lozano, 1998).

The primary types of PD include idiopathic Parkinson's disease, which accounts for the majority of cases, and secondary Parkinsonism, which results from known causes such as medications, toxins, or other neurological disorders (Kalia & Lang, 2015).

The cardinal signs and symptoms of PD include tremor at rest, bradykinesia (slowness of movement), rigidity, and postural instability (Jankovic, 2008). Non-motor symptoms such as sleep disturbances, autonomic dysfunction, mood disorders, and cognitive impairment are also common and contribute significantly to the disease burden (Chaudhuri et al., 2006).

Genetically, PD is associated with mutations in several genes, including SNCA, LRRK2, PARK2, PARK7, and PARK13 (HTRA2). Ongoing research aims to develop neuroprotective strategies and gene therapies to address the underlying causes of PD, with studies on genes providing insights into mitochondrial dysfunction and potential therapeutic targets (Klein & Westenberger, 2012).

Modern treatment strategies for PD primarily focus on managing symptoms. The cornerstone of treatment is the administration of levodopa, often combined with carbidopa to enhance its efficacy and reduce side effects. Other treatments include dopamine agonists, MAO-B inhibitors, and deep brain stimulation (DBS) for advanced cases (Hammer et al., 2010). Compared to dispersible levodopa treatment, a single dose of

Mucuna pruriens from roasted seeds exhibits strong anti-Parkinsonian effects in 18 patients with advanced Parkinson's disease (Cilia et al., 2017).

1.12 *Kampa vata* and Parkinson's Disease

Basavarajeeyam, an 18th-century treatise by Basavaraju, mentions kampa vata as a disease condition with cardinal symptoms similar to Parkinson's disease.

"करपादतले कम्पो देहभ्रमणदुखिते निद्राभग्नो मतिःक्षीणा कम्पवातस्य लक्षणम्।"

(Ba.ch-6)

Basavarajiyam has described detailed symptomatology of *Kampavata* (Sarvanga Kampa vata) as "*Karapadatalekampa*" (tremors in hands and legs), *Deha bhramana dukhite* (difficulty in bodily movements or rombergism), *Nidra bhanga* (insomnia) and *Kshina Mati* (impairment of intellect or memory loss) (Nilakantha kotturu, 2008) which comes in close relation with the symptoms of Parkinson's disease where the major clinical manifestations are tremors, rigidity, akinesia, and postural disturbances.

"एकबाहुप्रकम्पच्च विकारच्चापि देहिनाम् महादुखम् दिवरात्रौ बाहुकम्पस्य लक्षणम्।"

(Ba.ch-6)

Tremors occur in one arm, they persist throughout the day and night, causing significant difficulty for the individual, which is an early symptom of Parkinson's disease. Many studies in Parkinson's management have shown a significant effect of popular medicinal plants like MP.

1.13 Introduction to *Drosophila melanogaster*

Drosophila melanogaster, or the fruit fly, has been a pivotal model organism for over a century due to its short life cycle, ease of breeding, and well-understood genetics. Its genome, which shares significant homology with humans, makes it invaluable for studying genetic and developmental processes (Bellen et al., 2011). This model continues to be essential in biological research, offering insights into both basic biology and complex human diseases.

1.14 *Drosophila melanogaster* as a model organism

Neurodegenerative disorders, often idiopathic, have been associated with multiple genetic factors, prompting investigations into their genetics and molecular mechanisms (Rubin et al., 2000). Animal models have played a pivotal role in these studies, benefiting from advancements in genetic engineering that enable precise modifications such as gene knockout, chromosomal locus alteration, and creation of point mutations and copy number variants (Bier, 2005).

Drosophila melanogaster, has been instrumental as a model organism in genetic research for over a century, owing to its robust genetic toolkit and short life cycle (Bier, 2005). Its utility extends to modelling various neurodegenerative diseases due to genetic homology with humans and a brain structure composed of specialized substructures akin to humans (Bier, 2005).

For instance, the Drop-dead gene, identified through early genetic screens in *Drosophila* for abnormal behaviour, underscores its relevance in neurodegenerative studies (Konopka & Benzer, 1971). *Drosophila* 's genetic toolkit includes advanced techniques like transgenesis, RNA interference (RNAi), and CRISPR/Cas9 genome editing, enabling precise gene manipulation (Gratz et al., 2015). *Drosophila* shares over 77% homology with genes implicated in human diseases, making it an ideal model for investigating complex disorders like Parkinson's disease (PD) (Bier, 2005).

1.15 *Drosophila melanogaster* as a model organism in Parkinson's disease

Studies in *Drosophila* have contributed significantly to understanding PD pathogenesis, mechanisms of neurodegeneration, and potential therapeutic interventions due to its genetic tractability and evolutionary conservation of disease-related genes and pathways. Genetic manipulation in *Drosophila* has elucidated the role of key genes such as α-synuclein, Parkin, and PINK1 in PD-related neurodegeneration (Feany & Bender, 2000). *Drosophila* models have also facilitated drug screening and discovery efforts aimed at identifying compounds that can alleviate PD symptoms or modify disease progression (Mishra & Tiwari, 2021). Overall, *Drosophila melanogaster* continues to provide valuable insights into the complex molecular and cellular mechanisms underlying Parkinson's disease.

1.16 *park^{13}* mutant *Drosophila melanogaster*

park^{13} mutant refers to a strain of *Drosophila melanogaster* that carries a mutation in the gene homologous to the human *HTRA2* gene. Mutations in the HtrA2 gene, also designated as PARK13, which lead to the loss of its protease activity, have been associated with Parkinson's disease (PD) (M'Angale & Staveley, 2017), making it an essential model for studying PD pathogenesis.

1.17 Fecundity as a read out in *Drosophila melanogaster*

Fecundity, the reproductive capacity of an organism, is a vital metric studied extensively in *Drosophila melanogaster*. It serves as a key indicator of overall health and fitness, reflecting the impact of genetic mutations, environmental factors, and experimental conditions on reproductive success. Research in *Drosophila* has elucidated the molecular mechanisms underlying fecundity, including hormone signalling pathways, reproductive behaviour, and oogenesis (Chapman et al., 1995). Studies have also examined age-related declines in reproductive performance and the effects of dietary and pharmacological interventions on fertility, highlighting *Drosophila* as a valuable model for understanding reproductive biology in various contexts.

2.Materials and Methods

2.1 Ayurveda literature review on *Kapikacchu* (*MP)*

A comprehensive literature search was conducted using journals published in Ayurveda by institutions such as CCRAS, the e-Samhita database, and other relevant digital sources. Keywords such as "*Kapikacchu*", "Atmagupta", "Kandura", "Swayamputa," "Swagupta," "Languli," and "Rsyaprokta" were utilized for the search. Additionally, classical Ayurvedic texts, including the Brihat Trayee (Charaka Samhita, Sushruta Samhita, and Ashtanga Hridaya) and Nighantus (Bhava Prakasha, Kaiyyadeva Nighantu, Dhanwantari Nighantu, and Shodala Nighantu), were thoroughly reviewed. Relevant data were meticulously extracted, focusing on the pharmacological properties (Rasa, Guna, Virya, Vipaka), therapeutic uses, and synonyms of *Kapikacchu*. The extracted data were systematically compiled and compared to identify commonalities and differences across the texts and to understand the properties, suggested uses and therapeutic benefits of *Kapikacchu*.

2.2 Drosophila studies

2.2.1 Media composition (1000ml)

Composition	**Normal diet**	**Medicine diet**	**Medicine diet**
Corn flour	80g	80g	80g
Sugar	60g	60g	60g
Yeast Extract Powder	30g	30g	30g
Agar	8	8	8
Autoclaved distilled water	1000ml	1000ml	1000ml
Benzoic acid	7ml	7ml	7ml
Orthophosphoric Acid	6ml	6ml	6ml
Propionic acid	4ml	4ml	4ml
Kapikacchu choornam (Vaidyaratnam) Batch No. 23A0728		0.68g	1.36g

2.2.2 Preparation

The ingredients listed in the table above were weighed. Corn flour, sugar, yeast extract powder, agar, and autoclaved distilled water were thoroughly mixed and cooked in a pressure cooker until one whistle. After the steam subsided and the mixture reached the ambient temperature, all three acids were added and mixed thoroughly. For the medicinal media, the powder was diluted with the required amount of water and then added to the prepared media. The media was subsequently dispensed into the respective vials and bottles using a 10 ml syringe.

2.3 Fly husbandry

For the experiments, *CS*, and *Park* ^{13} strains of *Drosophila Melanogaster* were used, with the w*;;park13/TM6B,Tb, flies sourced from National Centre for Biological Sciences (NCBS). The flies were reared in a controlled environment, maintaining a constant temperature of 25°C in an incubator. Humidity levels were regulated at 60–65%. They were exposed to a 12-hour light and 12-hour dark cycle, mimicking the natural diurnal rhythm, to ensure optimal conditions for their growth and development (Markstein, 2018). The flies were kept in glass bottles and vials, and they were flipped every alternate day to prevent overcrowding.

2.4 Generation of ELS flies

To generate Early Life Starvation adult flies, a laboratory strain of *CS* flies was allowed to lay eggs for a 1-hour period, which were then allowed to mature for ~90 hours. Subsequently, L3 larvae were cleaned, and transferred to either "Normal Food" or food containing 100 mM sucrose (starvation media). The normal food or control diet fed eclosed flies are called the control flies and starvation media flies are called ELS flies. After eclosion, the adult flies were aged on normal food, with 25-30 adults per vial (Patil et al., 2022).

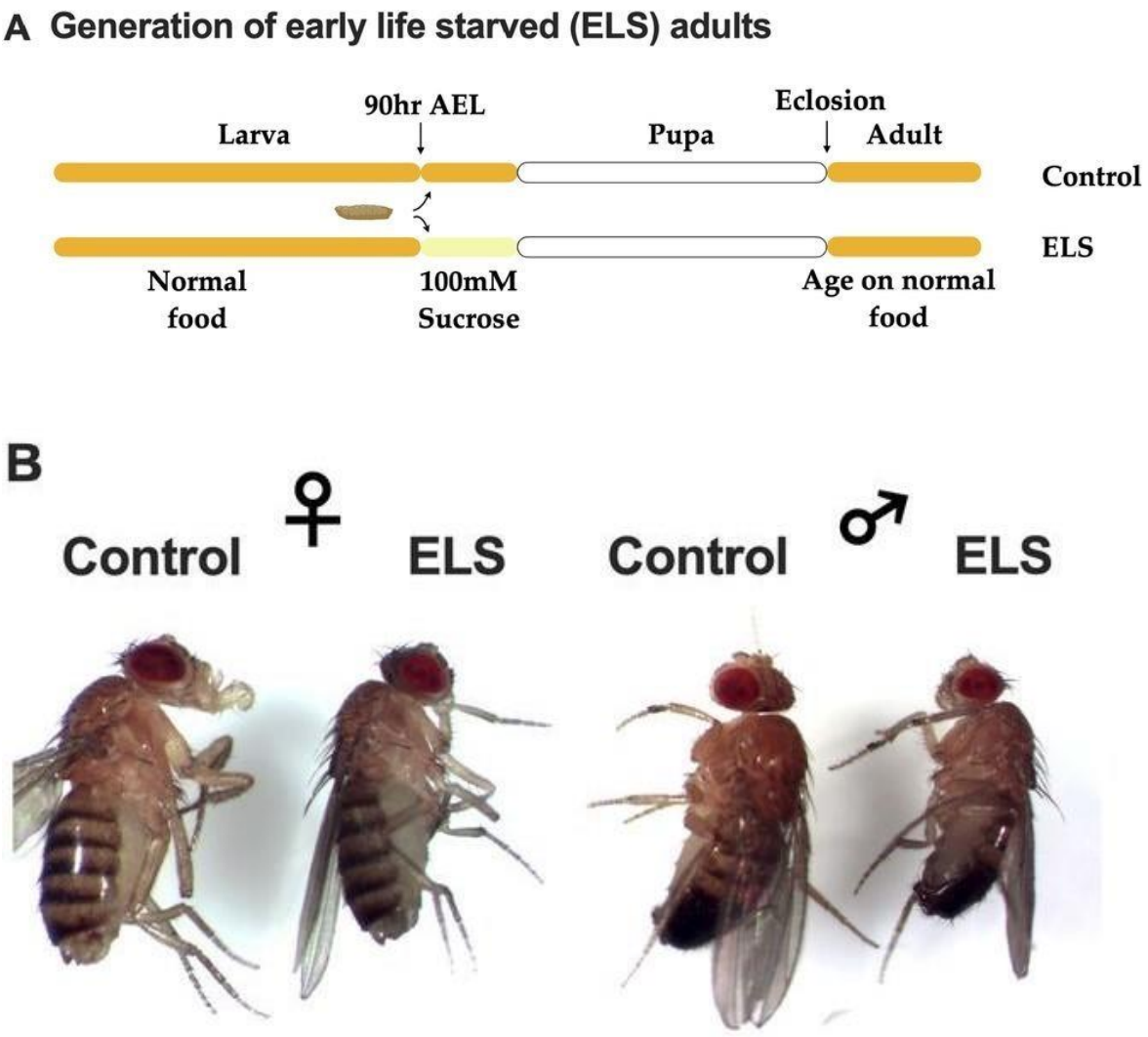


Figure 2.1- a)Process of generation of early life starved (ELS) and control flies . b) Showing the difference in appearance of male and female control and ELS flies (Patil et al., 2022).

2.5 Generation of *park13*/+ flies

The *park13* mutant fly was genotyped as *w*;;park13/TM6B,Tb*, where *TM6B* represents the balancer chromosomes expressing the dominant Tubby (Tb) phenotype. This mutant was generated through the deletion of the parkin gene.

Virgin female *CS* (Canton Special) flies, male *park*^{13} flies, and male *CS* flies were collected for the experiment. The *CS* flies served as the control group, while *park*^{13}/+ mutants were maintained as heterozygous as the heterozygous gene encoding the protein is the same.

From the crosses, the probability of obtaining *park*^{13}/+ progeny was calculated to be 50% using a Punnett square. The F1 generation larvae were collected 4-5 days post-cross. The desired progenies were sorted by subjecting them to water stress and eliminating those expressing the balancer marker, Tubby (Tb). Approximately 25 to 30 larvae were moved into vials with a normal diet. Similarly, wild-type larvae were also collected. This method ensured the removal of the balancer chromosome and the generation of the desired *park*^{13} mutant flies for the experiments.

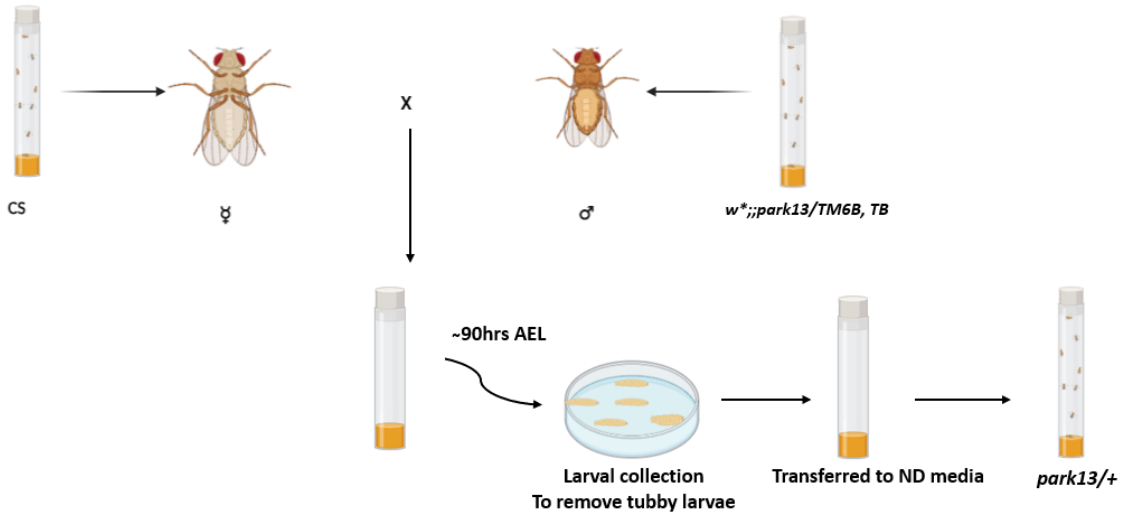


Figure 2.1- Schematic representation of generation of *park*^{13}/+ flies.

AEL- After egg laying, ND- Normal diet

2.6 Metabolic assay

To understand lipid and protein content on the fly. The assay measures triglyceride levels by detecting the glycerol released during an enzymatic reaction with lipase. One mole of glycerol is equivalent to one mole of triglyceride.

BCA (Bicinchoninic acid) assay is used for colorimetric detection and quantitation of total protein in the sample.

Materials required;

- TAG standard
- TAG buffer
- 0.2% Tween-20
- Nice water

- Weighing balance
- 1.5ml microcentrifuge tubes
- Micropipettes
- 96-well plate
- Manual homogenizer
- Heat block
- Centrifuge
- Microplate spectrophotometer
- Incubator

The assay was performed on the whole flies, with each sample containing 3 adult flies.

Procedure;

The flies were first sorted by sex on ice and weighed. Subsequently, three flies were placed into each microcentrifuge tube. The flies were then kept at -80°C for 10 minutes for killing. Following this, 200 µL of 0.2% Tween-20 was added to each centrifuge tube. The flies were homogenized using a manual homogenizer. An additional 300 µL of 0.2% Tween-20 was added, and the samples were incubated on a heat block at 70°C for 10 minutes for enzyme inactivation. The samples were then centrifuged at 4000 rpm for 5 minutes at room temperature. Finally, 200 µL of the supernatant was collected into 1.5 mL microcentrifuge tubes.

2.7 TAG assay- with benesphera avantor kit;

The standard triglyceride solution was diluted (1:1) with nice water and the reaction mixture were as follows:

Solution	**Blank**	**1**	**2**	**4**	**8**	**50µl (Sample)**
0.2% tween-20 (µl)	50	49	48	46	42	0
Enzyme buffer mix (µl)	150	150	150	150	150	150
Total (µl)	200	200	200	200	200	200

Readings were taken at a wavelength of 546 nm.

BCA assay- Bovine Serum Albumin (BSA), 1 mg/mL was used as the standard to estimate the sample protein concentration.

Sample was diluted (1:1) with 0.2% tween-20.

The reaction mixture was as follows:

Solution	Blank	1	2	4	6	8	10	100µl (Sample)
0.2% tween-20 (µl)	10	9	8	6	4	2	0	0
Enzyme buffer mix (µl)	80	80	80	80	80	80	80	80
Total (µl)	90	90	90	90	90	90	90	90

Readings were taken at a wavelength of 562 nm.

2.8 Fecundity assay;

The fecundity assay was conducted on *CS* (Canton special), *ELS* and *Park* ^{13} strains of *Drosophila Melanogaster*, with groups fed and not fed on medicinal media.

2.8.1 Fecundity on *park*^{13}/+ and +/+;

Following a 2-day maturation period post-eclosion, the flies were fed from the 3rd day onwards on either a medicinal diet (at two different concentrations) or standard corn flour media as a control.

Fecundity assay was performed on two age groups 1) 5th, 6th, and 7th days post-eclosion. 2) 19th, 20th, and 21st days post-eclosion, with the flies continuously fed on the medicinal diet throughout this period.

2.8.2 Fecundity on *ELS* and +/+;

For measuring fecundity in control and ELS flies, the flies fed on normal corn diet for 5 days post eclosion and then with medicine diet for next 7 days.

The experiments were conducted using cut vials containing the respective media to facilitate accurate egg counting.

Material required;

- Cut vials
- Insulation tape
- Cotton plugs
- Click counter
- Stereo microscope
- Ice and ice pads
- Soft brush
- Normal corn diet and medicine media

Method;

Normal corn diet and medicinal media were prepared as outlined in the table above. The cooked media was poured into cut vials and allowed to cool, after which the upper part of the vials was sealed with insulation tape. Three vials were prepared for each strain and concentration, ensuring the number of females to male ratio is 2:1. The flies were transferred to the cut vials following a 24-hour acclimatization period. They were then transferred to new cut vials every 12 hours over a period of three consecutive days (72 hours). Egg counting was performed using a stereo microscope and a click counter. The number of females in each vial was recorded, and data on egg counts were calculated based on the number of females present in each vial.

2.9 Paraquat induced oxidative stress

Material required;

- 5% sucrose solution - 50 ml (autoclaved)
- Paraquat - 5 mM (1.28 mg/ml)
- Clean empty vials
- Absorbent cotton or filter paper cut into circles

Procedure

To start the experiment, sort the flies by sex and place 8-12 in each vial. Prepare empty vials one hour in advance, placing a thin layer of cotton or filter paper at the bottom. Add

150 µL of 5% sucrose solution to the control vials and 150 µL of paraquat solution to the experimental vials. Let the vials sit for 10 minutes to allow the solutions to absorb fully. Label the vials to differentiate between control and experimental groups, then transfer the sorted flies into the corresponding vials. Record the number of dead flies every 12 hours and regularly hydrate the vials with a syringe to ensure the flies have sufficient moisture.

2.10 Retrospective study on *Kapikacchu* use at I-AIM Healthcare centre

The study involved a retrospective review of patient data spanning five years (January 2019 to December 2023) from IAIM Healthcare Centre, utilizing the Hospital Management Information System (HMIS) and Electronic Health Record (EHR) system. Institutional Ethi*cs* Committee (IEC) approval was obtained with protocol number [TDU/IEC/15/2024/PR60]. The study focused on patients who were prescribed *Kapikacchu*, either alone or in combination formulations, and those diagnosed with 'Vatavyadhi-Kampa'. All those patients who had consulted from January 2019 to December 2023, prescribed with *Kapikacchu*was included in the study. Also those who are diagnosed as *Vatavyadhi- Kampa* in the Medical record for this 5 years were included in the study. Any record with incomplete description or unclear disease class was excluded from the study. Initially, data extraction involved filtering anonymized records of these patients from the HMIS and EHR databases.

Data analysis was conducted using Microsoft Excel 2019 (Version 2402), employing descriptive statisti*cs*. Various visualization tools within Excel were utilized to present the findings effectively, including charts, graphs, and tables.

3.Results and Discussion

3.1 Ayurveda literature review on *Kapikacchu*

3.1.1 History

The historical use of *Kapikacchu* (*Mucuna pruriens*) in traditional medicine lacks references in Vedic literature, with its documentation beginning from the Samhita period. The earliest references appear in Charaka Samhita (1000BC – 400 AD) (Bhavana & Shreevathsa, 2014), followed by significant mentions in Sushruta Samhita (6th century BC)(Loukas et al., 2010) and Ashtanga Hridaya (13th century) (Subhakta, 1997). However, these texts did not widely use the term *Kapikacchu*; instead, they referred to it by other names such as *Atmagupta*, *Swayamgupta,* and *Swagupta*. *Kapikacchu* is known by different names based on its properties, morphology, and indications.

Table 3.1 : Synonyms of *Kapikacchu* and their meaning in Ayurveda

Classical Sanskrit name	**Meaning of the name**
Atmagupta	By its self protecting nature with its hairs.
Ajada	Potent aphrodisiac
Durabhigraha	The fruits are difficult to handle
Vrishya	Acts as aphrodisiac
Languli	Shape of the legume resembles monkey's tail
Kapikacchu	Causes itching to monkeys
Markati	Hairy like monkey's tail
Vanshukari	Wildly growing climbers
Kandura	Hairs produce intense itching

Pravrishayana	Climber growing in rainy season
Suka simbhi	Pods with hairs
Kapiromaphala	Pod hair resembling monkey's hair
Dusparsha	Produce irritable sensation on touching
Svayamgupta	Plant is protected by hairs on fruits
Kacchura	Causes itching

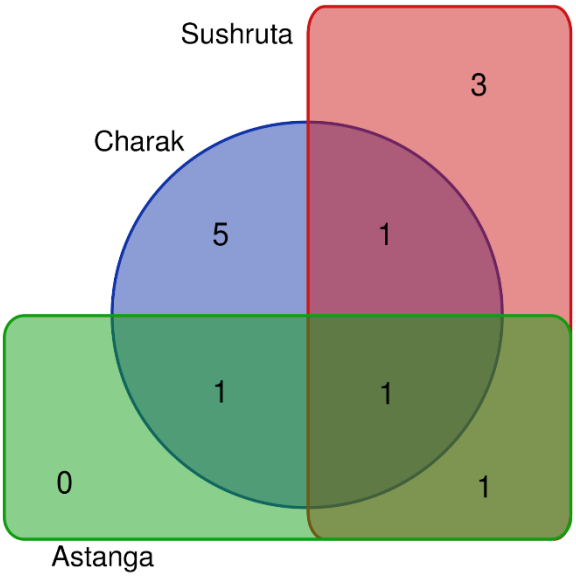


Figure 3.1: Different synonyms used in the Brihat trayee, plotted from the Table 3.2.

Table 3.2 : Major synonyms mentioned in Brihat trayee

Sl NO	Synonyms	Charaka	Sushruta	Ashtanga Hridaya
1	*Rishyaprokta*	*		
2	*Atmagupta Phala*	*	*	*
3	*Swayamgupta Phala*	*	*	
4	*Ajaphala*	*		
5	*Markadi*	*		
6	*Kapikacchu*	*		*
7	*Swagupta*	*		*
8	*Languli*		*	
9	*Gupta Phala*		*	
10	*Kushimbivali*		*	

In the Brihat Trayees, the term "*Kapikacchu*" is not used on the Sutra sthanas. In Caraka samhitha, word *Kapikacchu* is seen on the Chikitsa stana. On the chikitsa, nidana and uttara sthana's Vagbhata mentioned "*Kapikacchu*". Instead, synonyms like "*Atmagupta*," "*Swayamgupta*," and "*Swagupta*" are more frequently mentioned. The following Table 3.2 and Figure 3.1 illustrate some of the unique and similar synonyms used by the Acharyas

Charaka, Sushruta, and Vagbhata. The earliest mention of the name kapikacchu is in the Chikitsa sthana of Caraka samhitha which is redacted by Drdabala.

3.1.2 CLASSIFICATION OF *KAPIKACCHU*

Different Acharyas have mentioned Kapikacchu in various Ganas and Vargas according to its gunas or properties (Table 3.3). This shows, all the gana's mentioned here are having vatahara (that which can pacify vata dosa) property.

Table 3.3 : Classification of Kapikacchu according to different Acharyas

Text	***Gana/ Varga***
Charaka samhitha	*Balya* *Madhura Skanda* *Purisa Viranjaniya*
Sushruta samhitha	*Vidarigandhadi* *Mudgadivarga* *Kakolyadi*
Astanga Sangraha/ Astanga Hridaya	*Vidaryadi*
Bhavaprakasa Nighantu	*Guducyadi*
Kaiyadeva Nighantu	*Ausadhi*
Sodhala Nighantu	*Guducyadi, Laxmanadi*

3.1.3 Properties (*Rasapanchaka*) of *Kapikacchu* according to different Acharyas

According to the Ayurvedic Pharmacopoeia of India (API), *Kapikacchu* is characterized by the following general properties: *Rasa* (taste) as *Madhura* (sweet) and *Tikta* (bitter), *Guna* (qualities) as *Guru* (heavy) and *Snigdha* (unctuous), *Virya* (potency) as *Sita* (cooling), and *Vipaka* (post-digestive effect) as *Madhura* (sweet). However, there are

differing opinions among various Acharyas. For instance, Shodala Nighantu describes *Kapikacchu* as having *Laghu* g*una* (light), while Sushruta classifies it as having *Ushna virya (*hot potency). Despite these variations, the majority of Acharyas consistently highlight its *Brumhana* (nourishing) and *Vrushya* (aphrodisiac) properties as shown in the Table 3.4.

Table 3.4: Properties of Kapikacchu mentioned by different Acharyas and on API

RASAPANCHAKA	**S.S**	**D.N**	**K.N**	**BP**	**S.N**	**API**
RASA						
Madhura		+	+	+		+
Tiktha		+	+	+	+	+
GUNA						
Guru	+	-	+	+	+	+
Laghu					+	
Snigdha	+	-	-	+	+	+
Brimhana			+	+		
Vrushya		+	+	+	+	
Balya				+		
VIRYA						
Sita		+	+	-	+	+
Ushna	+					
VIPAKA						
Madhura		-	-	-	+	+
KARMA						
Vata-hara		+	+	+	+	+
Kapha-hara			+	+		+
Pitta-hara		+	+	+	+	+

S.S- Susrutha Samhitha, D.N- Dhanwantari Nighantu, K.N- Kaiyyadeva Nighantu, B.P-Bhavaprakasha Nighantu, S.N- Shodala Nighantu, API-Ayurveda Pharmacopoeia of India

3.2 *Drosophila* studies

3.2.1 Metabolic assays- TAG and BCA;

Metabolic assays, including TAG (triacylglycerol) and BCA (bicinchoninic acid) assays, were performed to determine if the *Brumhana* (nourishment) and *Balya* (strengthening) properties attributed to the drug have any relation to the total triacylglycerol and protein levels in the fly.

3.2.1.1 TAG assay on *CS (+/+)* flies - 5 days of feeding

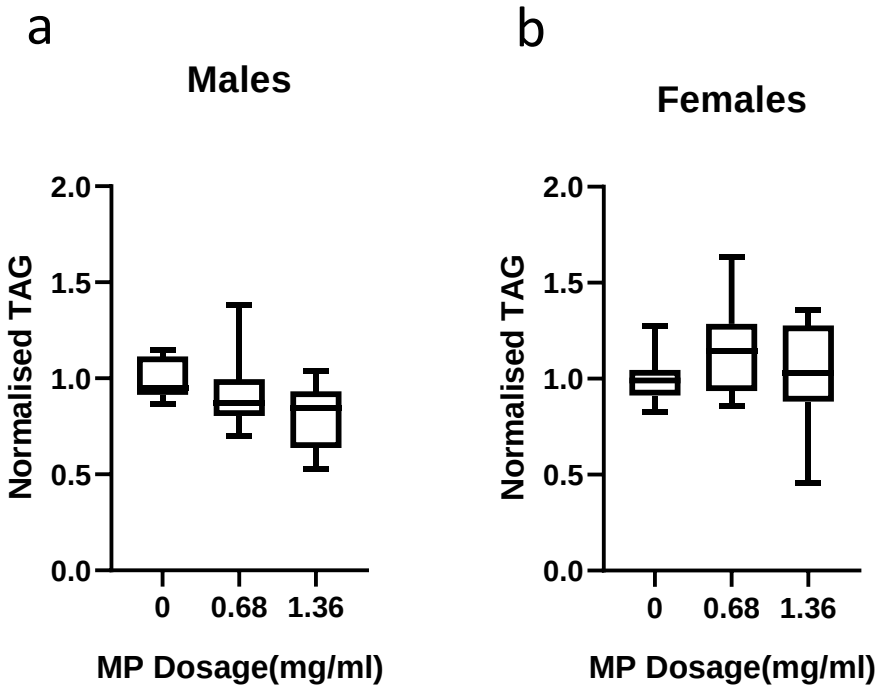


Figure 3.2 : Normalised TAG/weight quantified for 3 dosages of MP, n=10*3 flies 8 day old *CS* males and females were taken for the experiment.

3.2.1.2 TAG assay on *park*^{13}/+ flies - 5 days of feeding

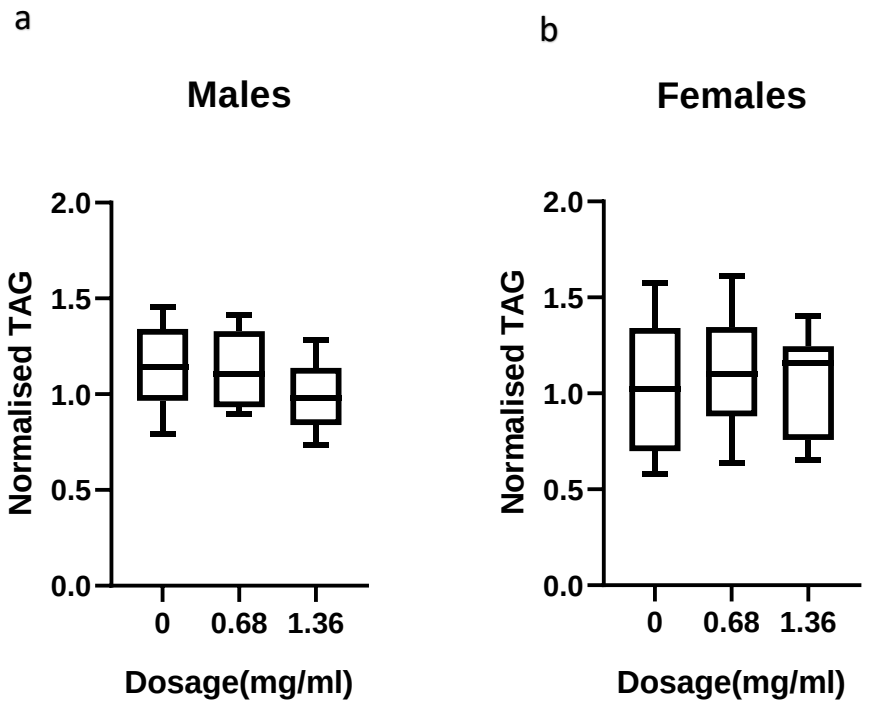


Figure 3.3 : Normalised TAG/weight quantified for 3 dosages of MP, n=10*3 flies 8 day old *park*^{13}/+ males and females were taken for the experiment.

When comparing the TAG levels of CS and park13/+ flies fed on MP diet, we did not observe any significant changes in the flies when compared to the flies fed on the ND diet. This suggests that feeding on MP diet, both 0.68mg/ml and 1.36mg/ml, for 5 days did not affect the TAG levels in the control or mutant flies.

3.2.1.2 TAG assay on *CS (+/+)* flies- 10 day post-treatment:

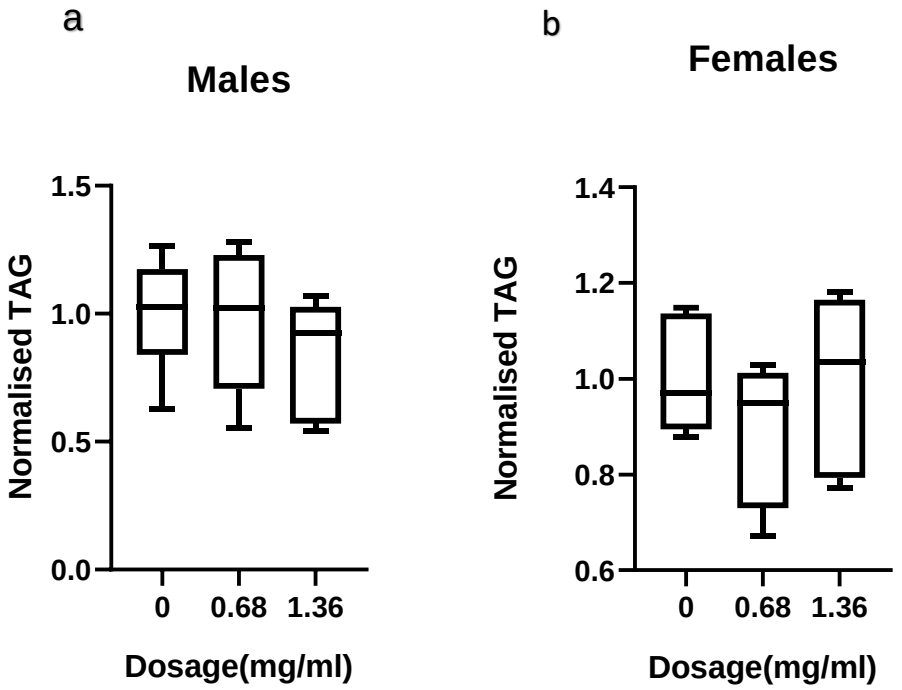


Figure 3.4 : Normalised TAG/weight quantified for 3 dosages of MP, n=6*3 flies 13 day old *CS* males and females were taken for the experiment.

Upon feeding MP diet for 10 days, in both males and females, the *CS* flies did not have any changes observed in their TAG levels on both 0.68mg/ml and 1.36mg/ml when compared to flies fed on ND media.

3.2.1.3 TAG assay on *CS(+/+)* flies- 15 day post-treatment:

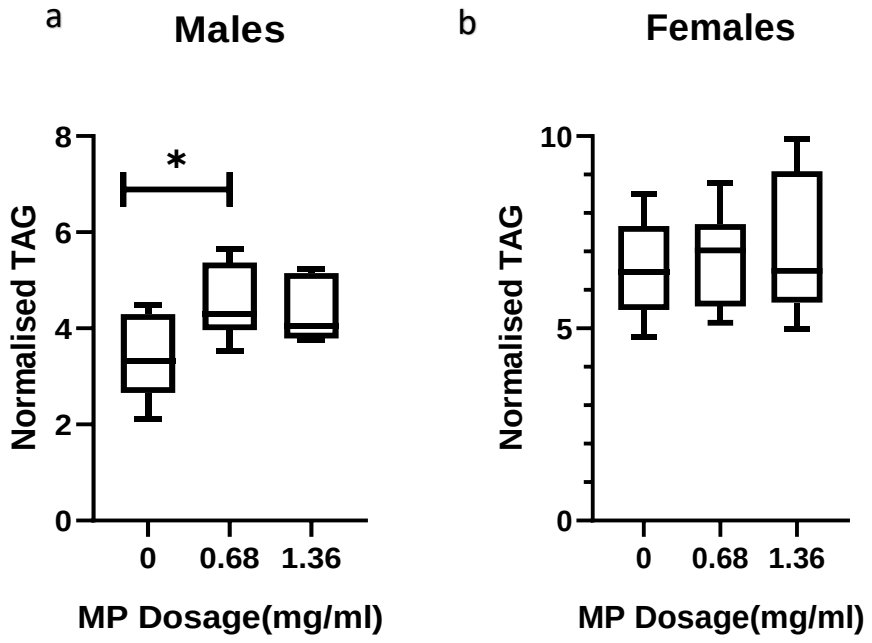


Figure 3.5 : Normalised TAG/weight quantified for 3 dosages of MP, n=6*3 flies 18 day old *CS* males and females were taken for the experiment.

Upon feeding for 15 days on the medicine media, we observed a significant increase in TAG levels in CS flies fed on a 0.68mg/ml MP diet, in males and a similar trend though not significant in females when compared to flies fed on ND diet. Our findings indicate that a short-term feeding regime of 5 or 10 days does not affect TAG (triacylglycerol) levels, while a long-term feeding of 15 days with the MP diet is necessary to modulate TAG levels.

3.2.1.4 Temporal analysis of TAG on 5, 10, and 15 days post-treatment;

Additionally, we were interested in understanding how TAG levels differ with age and long-term feeding. For this, *CS* flies were fed on medicine (*Mucuna pruriens*) diet for 5, 10 and 15 days after giving them a maturation period of 2 days.

Comparative analysis of TAG on *CS (+/+)* male flies

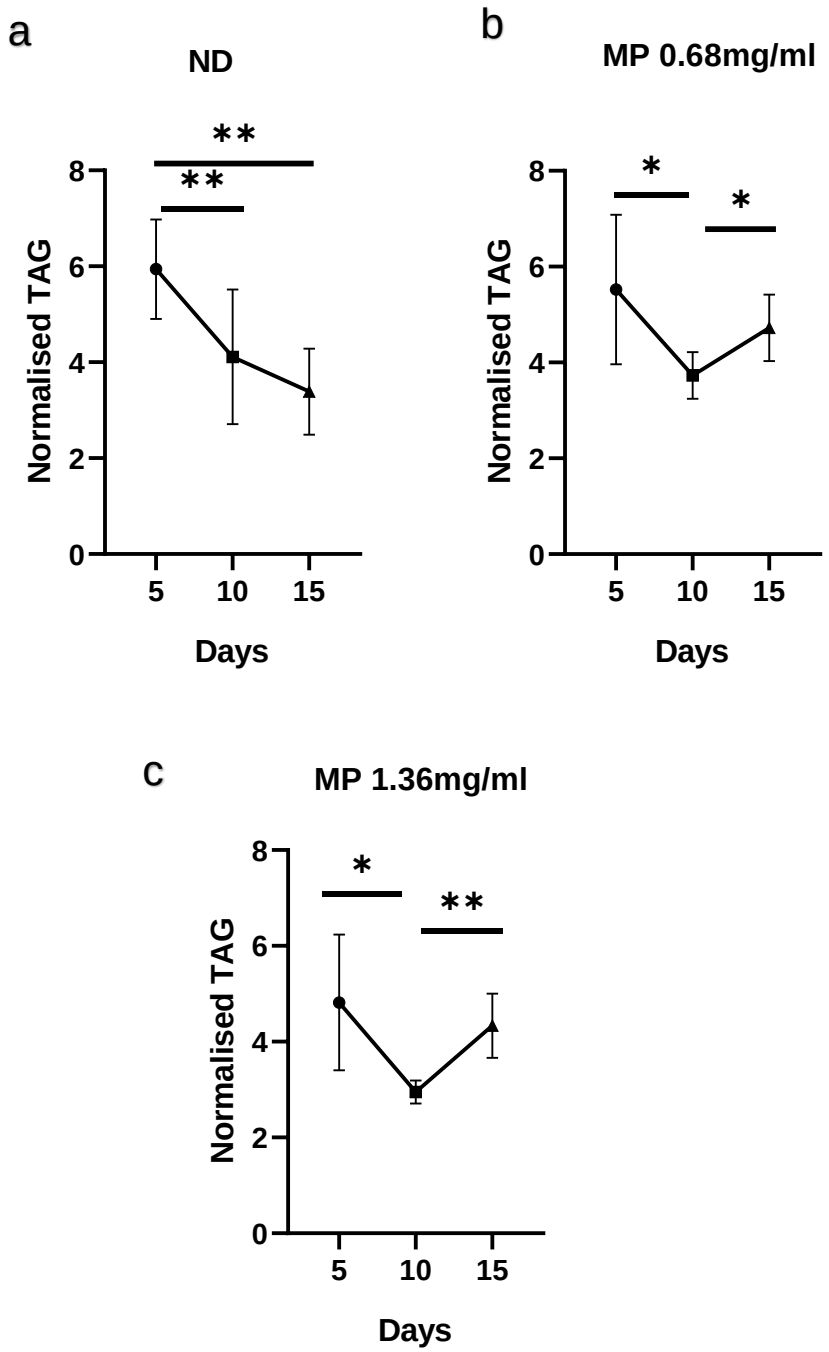


Figure 3.6*:* Changes in TAG levels over time, during the period of 5, 10 and 15 days at two different concentrations of MP (0.68 mg/ml and 1.36 mg/ml) in *CS* males when normalised with weight. n=6*3 flies. a) *CS* males fed on Normal diet, b) *CS* males fed on 0.68mg/ml MP diet, c) *CS* males fed on 1.36mg/ml MP diet. Unpaired t-test for Statistical analysis-$p<0.05$.

Comparative analysis of TAG on *CS (+/+)* female flies

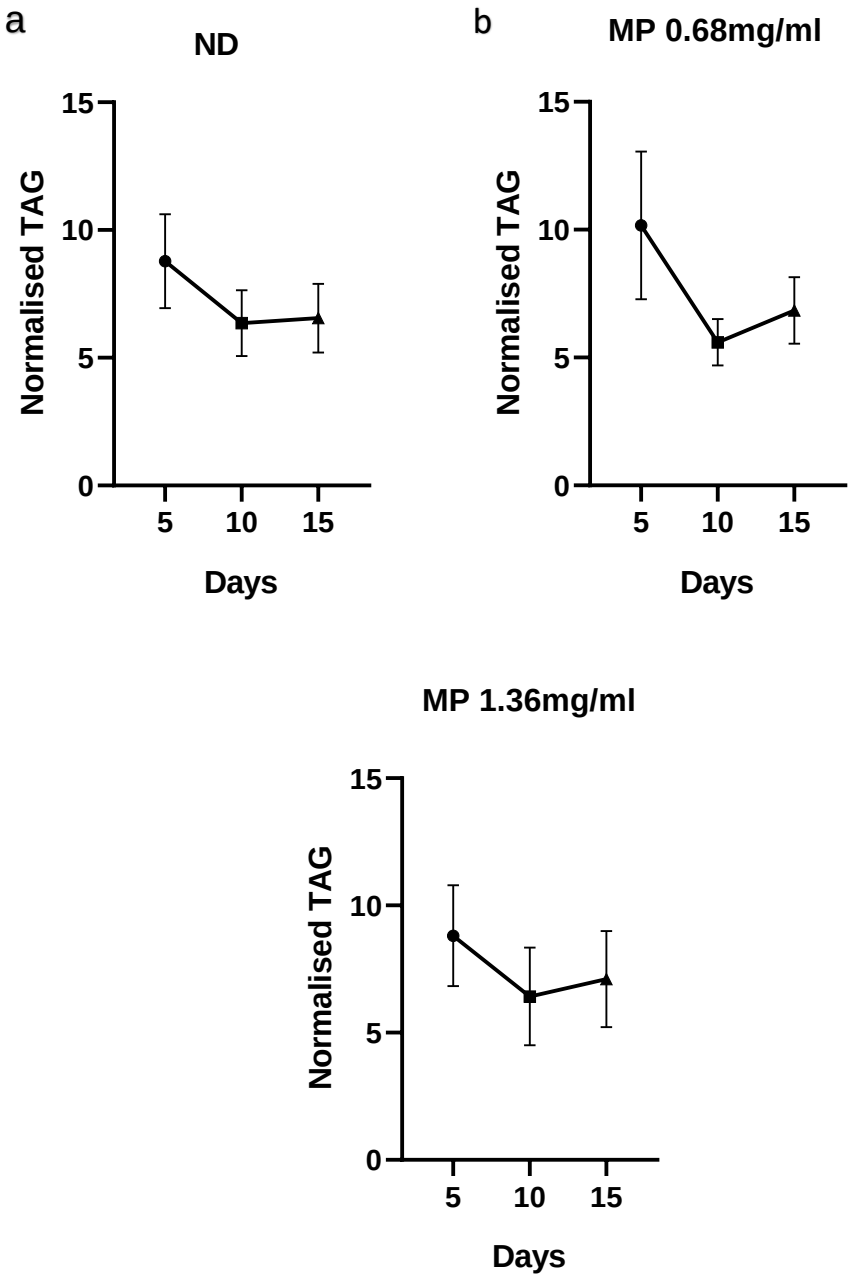


Figure 3.7*:* Changes in TAG levels over time, during the period of 5, 10 and 15 days at two different concentrations of MP (0.68 mg/ml and 1.36 mg/ml) in *CS* females when normalised with weight. n=6*3 flies. a) *CS* females fed on Normal diet, b) *CS* females fed on 0.68mg/ml MP diet, c) *CS* females fed on 1.36mg/ml MP diet. Unpaired t-test for Statistical analysis.

From the temporal analysis of TAG levels, we observed an initial decrease in TAG levels during the first 10 days of feeding, both in the normal diet group and in the groups fed with *Kapikacchu choorna* (MP) at different concentrations. This trend was consistent in both male and female CS flies. After this initial decline, TAG levels improved, showing an increase by the 15th day of feeding compared to the normal diet group.

In male flies, there was a significant increase in TAG levels. Although it was not statistically significant, female flies also exhibited a similar trend. The observed changes in TAG levels suggest that *Kapikacchu choorna* may exert its full metabolic effects over a longer period, highlighting its potential for enhancing lipid metabolism and overall nourishment.

3.3 Fecundity assay

To evaluate the *Vrushya* (aphrodisiac) property of *Kapikacchu*, a fecundity assay was performed using two different doses of *Kapikacchu choorna*. This assay was conducted on Parkinson's mutant (*park^{13}/+)* flies and early-life malnourished (ELS) model flies, with wild-type (*CS*) flies serving as the control group.

3.3.1 Short term fecundity on *CS* and *park^{13}* flies

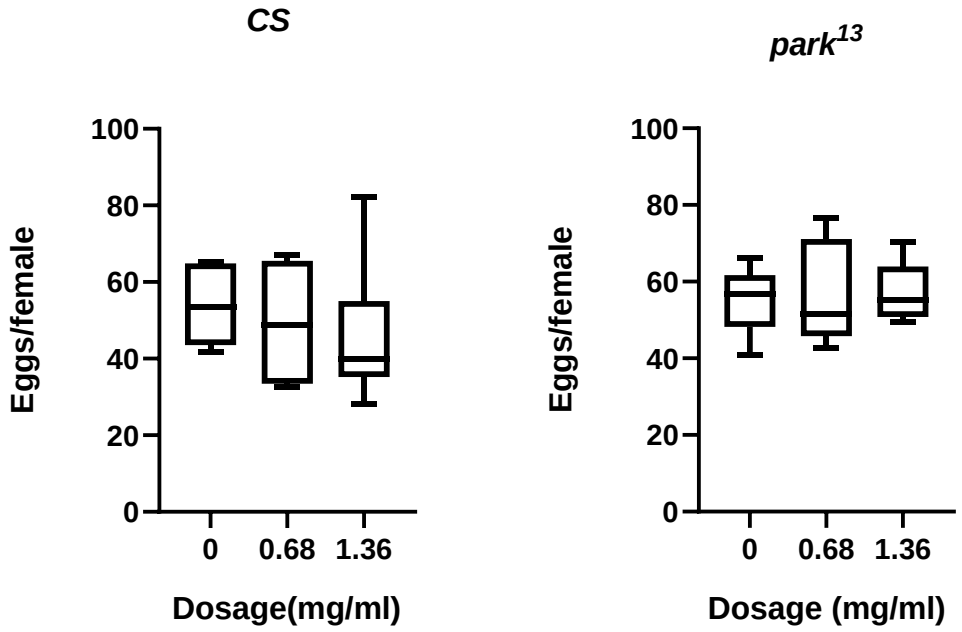


Figure 3.8*:* Fecundity of *CS* and *park^{13}* flies quantified for 3 dosages of MP. Fecundity was calculated on 5th,6th, and 7th day of eclosion. n=6 vials. a) *CS* (+/+) flies, b) *park^{13}*/+ flies.

In *park^{13}*/+ and *CS* flies, no significant difference in fecundity was observed upon treatment with MP for a short-term feeding with a dosage of 0.68mg/ml and 1.36mg/ml. As described in the methodology part, flies were fed on the MP diet from 3rd day of eclosion.

3.3.2 Long term fecundity on *CS* and *park*^{13} flies

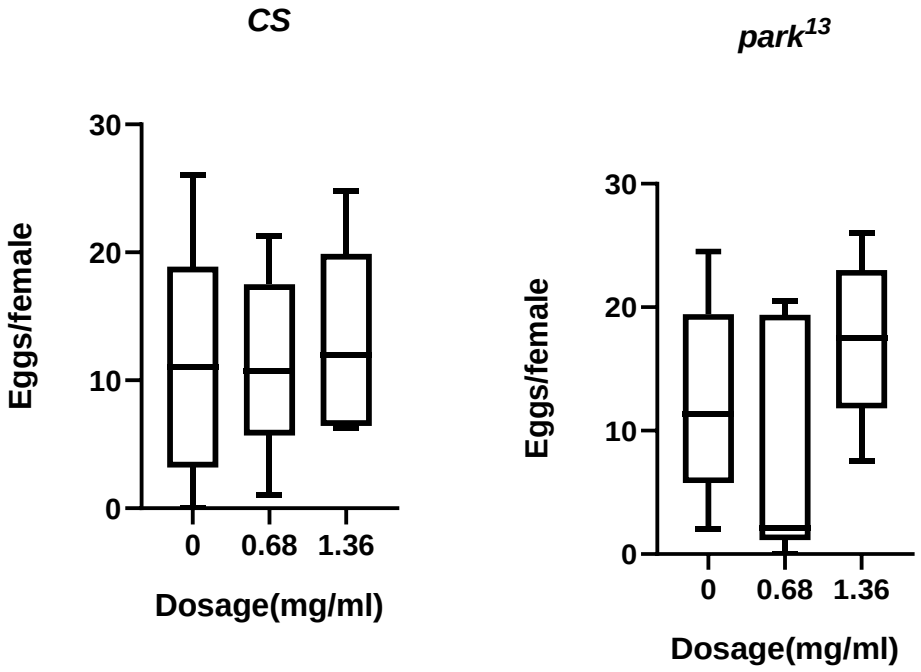


Figure 3.9 : Fecundity of *CS* and *park*^{13} flies quantified for 3 dosages of MP. Fecundity was calculated on 19th,20th, and 21st day of eclosion. n=6 vials.

In *park*^{13}/+ and *CS* flies, no significant difference in egg laying was observed upon treatment with *Mucuna pruriens* for a long-term feeding as mentioned on the methodology, with 0.68mg/ml and 1.36mg/ml.

3.3.3 Short term fecundity on ELS flies

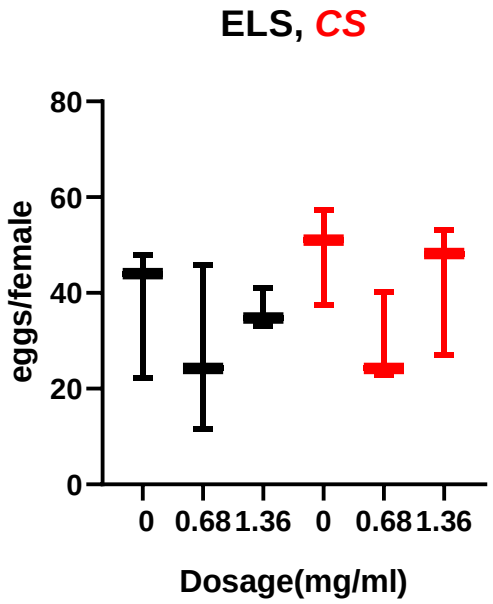


Figure 3.10 *:* Short- term fecundity of ELS compared with control (*CS)* flies on 3 dosages of MP. Fecundity was calculated on 5th,6th and 7th day of eclosion. n=3 vials.

ELS flies fed on ND diet were previously reported to have a reduction in the number of eggs laid when compared to control flies fed on ND diet. However, feeding of MP diet, both 0.68mg/ml and 1.36mg/ml, did not improve the egg laying in ELS flies when compared to the number of eggs laid by ELS flies fed on ND diet.

Taken together, our data suggests that feeding of MP does not affect the reproductive capability of the organism.

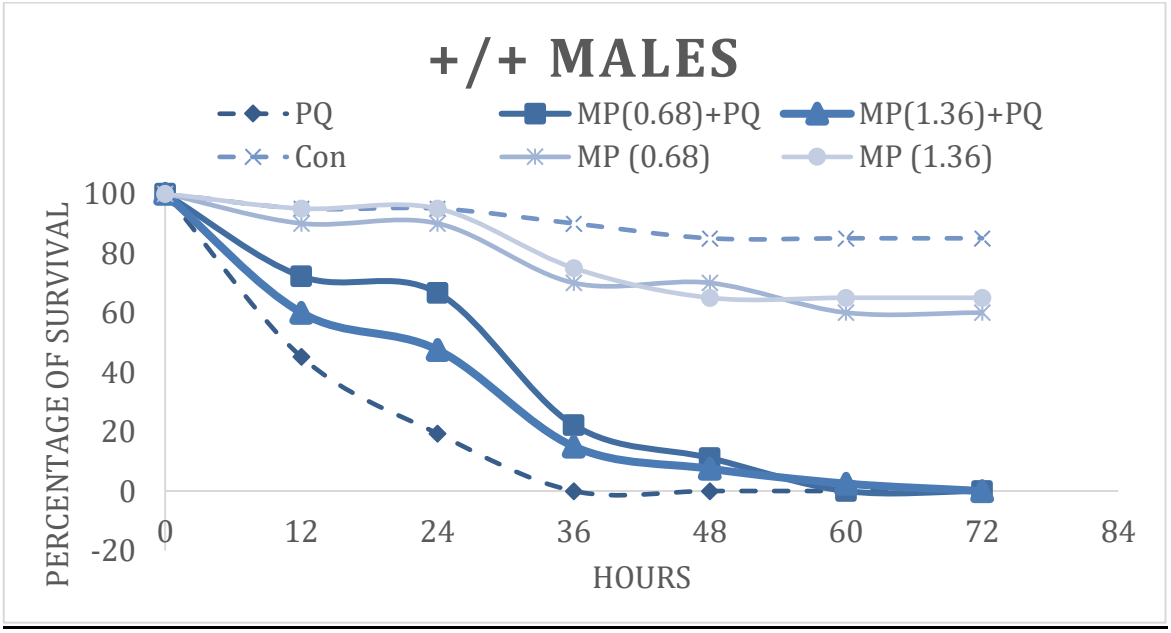
3.4 Paraquat induced oxidative stress

Paraquat, a redox-active herbicide, engages in redox cycling within cells, particularly in mitochondria. It accepts electrons from cellular reducing agents like NADPH, transferring

them to molecular oxygen and generating superoxide radicals, which in turn, form other reactive oxygen species such as hydrogen peroxide and hydroxyl radicals. Elevated levels of reactive oxygen species induce oxidative stress, causing damage to lipids, proteins, and DNA. This oxidative stress, coupled with mitochondrial dysfunction resulting from disruption of the electron transport chain and compromised ATP production, triggers cell death pathways, including apoptosis. Paraquat-induced oxidative stress can also cause inflammation and organ damage.

3.4.1 Paraquat induced oxidative stress in *CS* and *park*^{13} males

a



b

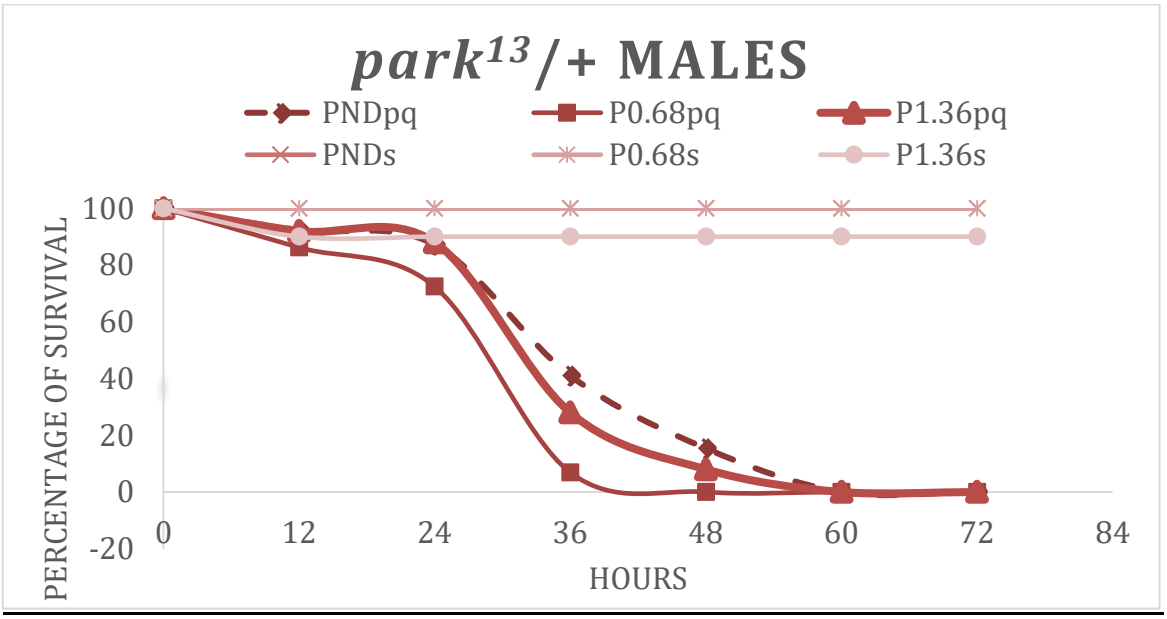


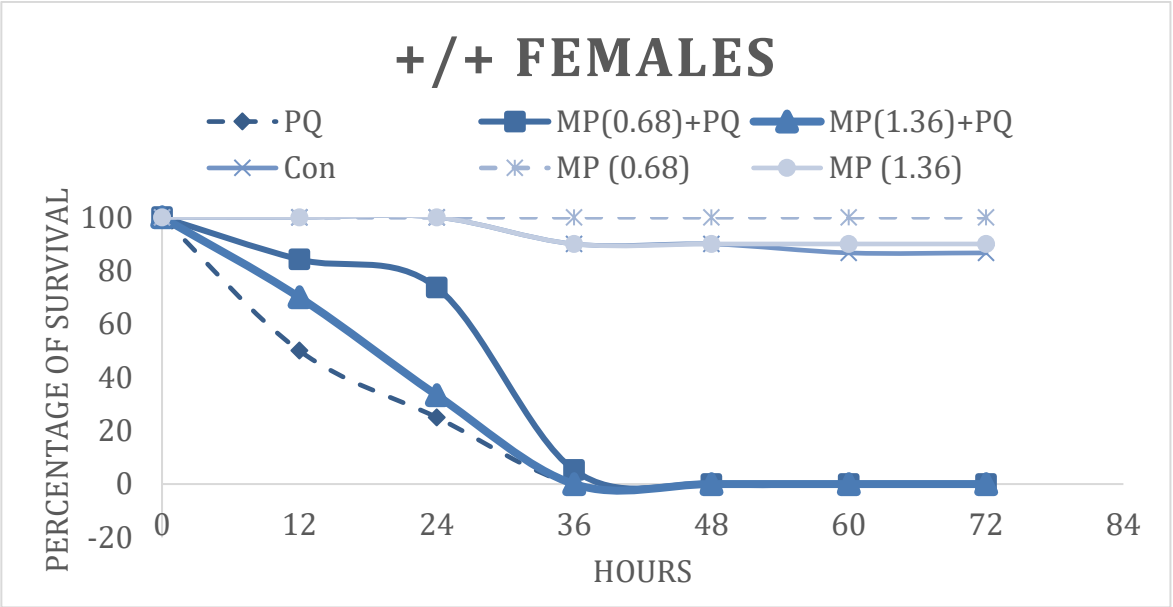
Figure 3.11 : Result for paraquat induced oxidative stress on post treatment of MP with two concentrations (0.68mg/ml and 1.36mg/ml). Light blue and brown coloured represent the flies fed on control media (sucrose). Dark lines represent the flies exposed to paraquat. Dash lines represents normal diet fed flies exposed to sucrose and paraquat. a) *CS* males, b) *park*^{13} males. Statistical analysis - Statistical analysis was performed using Kaplan-Meier estimate (log-rank test).

In male flies, *Kapikacchu* (MP) feeding improved resistance to oxidative stress in *CS* flies. Enhanced oxidative stress resistance was significant with a dosage of 0.68 mg/ml of MP.

However, this improvement was not observed in *park*^{13}/+ flies. 1.36mg/ml dosage of MP did not have any impact on dealing with oxidative stress, while 0.68mg/ml dosage of MP diet contributed to sensitivity to oxidative stress of *park*^{13}/+ flies.

Paraquat induced oxidative stress in *CS* and *park*^{13} females

a



b

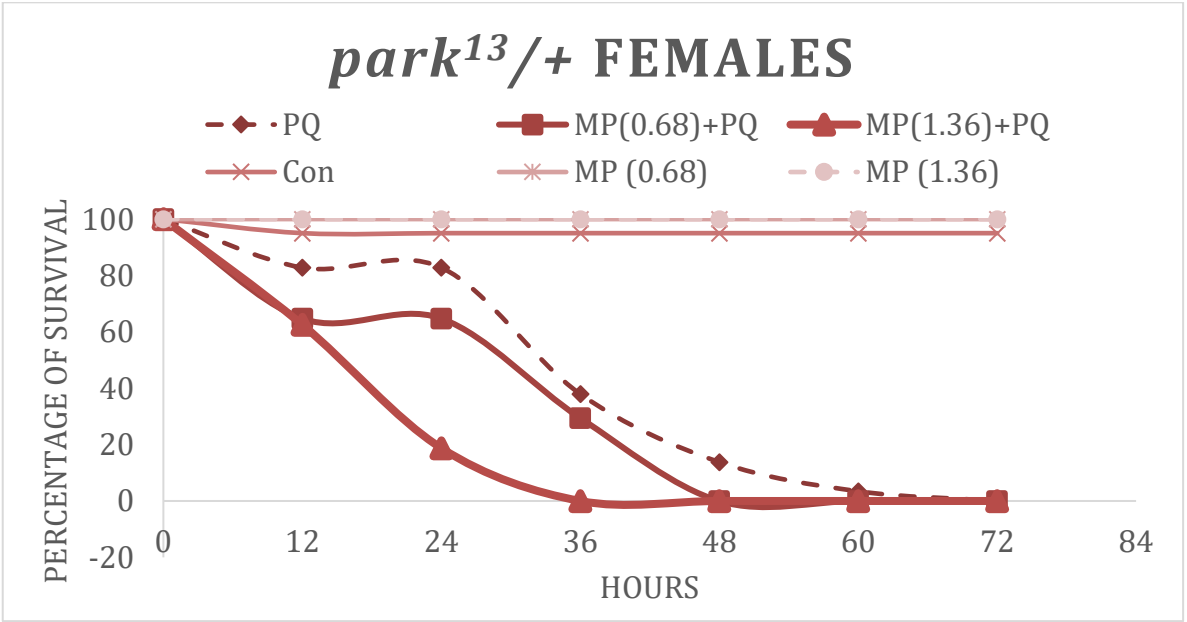


Figure 3.12 : Result for paraquat induced oxidative stress on post treatment of MP with two concentrations (0.68mg/ml and 1.36mg/ml). Light blue and brown coloured represent the flies fed on control media (sucrose). Dark lines represent the flies exposed to paraquat. Dash lines represents normal diet fed flies exposed to sucrose and paraquat. a) *CS* females, b) *park*^{13} females. Statistical analysis - Statistical analysis was performed using Kaplan-Meier estimate (log-rank test).

The oxidative stress resistance in *CS* females were found to improve only upon feeding 0.68mg/ml of MP diet and there was no significant improvement in dealing with oxidative stress upon feeding 1.36mg/ml of MP diet. While in *park13*/+ flies, the MP diet feeding showed no improvement in resisting to oxidative stress. A dose-dependent decline in survival was observed in these flies.

3.5 Retrospective study on *Kapikacchu* use at I-AIM Healthcare center

3.5.1 Patient Demographics and Prescription patterns of *Kapikacchu choorna*

A total of 265 medical record (MR) numbers were included in this study, all of whom had purchased Kapikacchu choorna from the I-AIM pharmacy. Initially, 581 MR numbers were reviewed. Through this analysis, 37 specific conditions were identified and sorted based on Ayurvedic indications and the recommendations provided by doctors regarding the prescribing conditions for Kapikacchu. After removing 314 MR numbers categorized as over-the-counter transactions without a doctor's prescription and duplicates, the final count was 265 MR numbers.

The age distribution of patients who purchased *Kapikacchu choorna* ranged from 18 to 97 years. Gender distribution showed a predominance of male patients (180), with their percentage being double that of female patients (87). This disparity indicates a higher utilization or recommendation of *Kapikacchu* among male patients.

The pie chart (Figure 3.10) provides a detailed distribution of the various conditions for which *Kapikacchu choorna* was prescribed. The largest segment, representing 40.1%, corresponds to patients diagnosed with Vaatavyaadhi – Kampa (~Parkinson’s disease), indicating that this condition is the most common reason for prescribing *Kapikacchu choorna*. Other significant conditions include various other *Vaatavyaadhi*’s (diseases caused due to the vitiation of *vata*). The chart also highlights the significant indication of *Kapikacchu choorna* for Klaibya (~erectile dysfunction), accounting for 8.6% of the prescriptions.

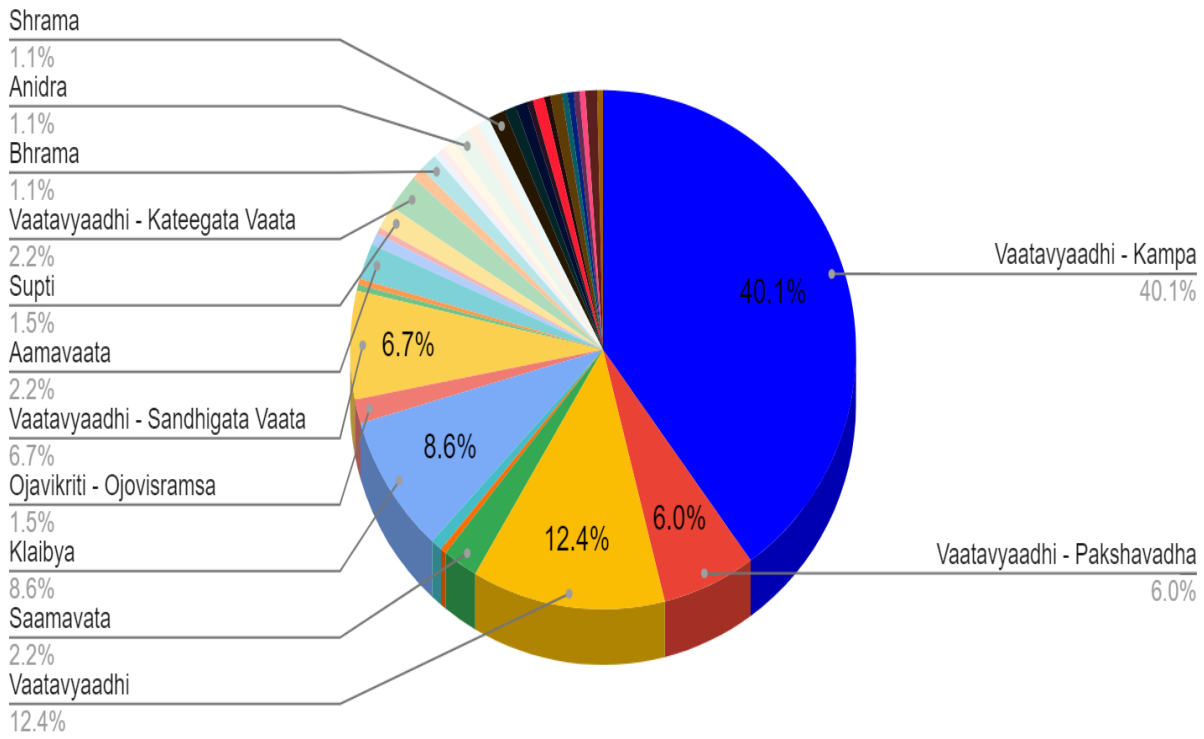


Figure 3.10 – Percentage of prescription of *Kapikacchu choorna* in various clinical conditions

Furthermore, the categorization of departments visited by these patients revealed a higher number of visits to the *Rasayanatantra* department- this department focuses on rejuvenation therapies and promoting overall health and longevity, which aligns with the traditional uses of *Kapikacchu* for its nourishing and aphrodisiac properties.

3.5.2 Patient Demographics and Prescription Patterns of Kampa vata (Parkinson's disease)

Over a five-year period, IAIM Hospital diagnosed 487 patients with Kampa Vata, who collectively made 1,357 visits. The patient demographic showed a higher prevalence of males, with 323 male patients compared to 164 females (Figure-3.11). The age distribution of these patients, ranging from 31 to 100 years old, revealed a peak incidence in the 71 to 80-year age group, followed by the 81 to 90-year age group. Significant numbers of patients were also observed in the 61 to 70 and 51 to 60-year age groups.

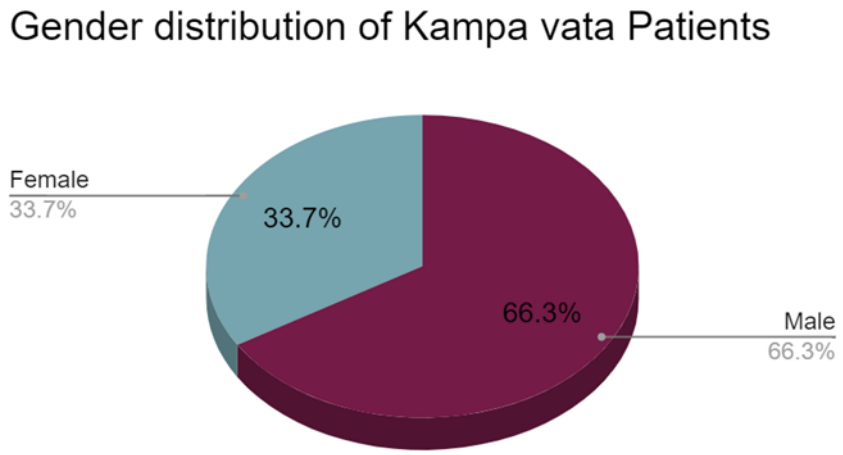


Figure 3.11: The pie chart illustrates the percentage distribution of male and female patients diagnosed with Kampa Vata.

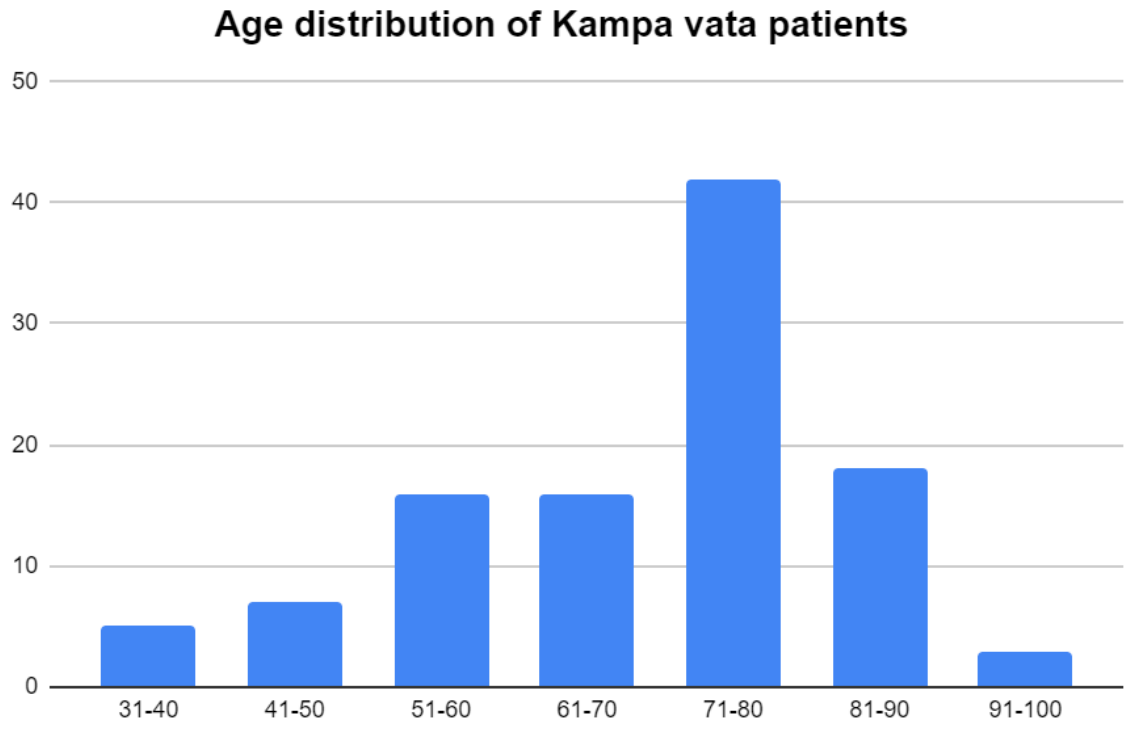


Figure 3.12: Shows age wise distribution of patients diagnosed as *Kampa vata*, where X-axis representing the age intervals and Y-axis representing the percentage of patients.

Out of the 487 patients diagnosed with Kampa Vata, 90 patients were prescribed *Kapikacchu*. Within this subset, the gender distribution was consistent with the overall

trend, with a higher number of male patients receiving the prescription. Specifically, 61 males and 29 females were prescribed *Kapikacchu*.

The data indicates a significant engagement with *Kapikacchu* in the treatment regimen for Kampa Vata, particularly among male patients. This pattern may reflect either a higher incidence of Kampa Vata in males or a greater propensity for prescribing *Kapikacchu* to male patients within the clinical practices. The detailed demographic breakdown and prescription patterns highlight the importance of *Kapikacchu* in managing *Kampa Vata* and underscore the need for further research into its gender-specific effects and overall efficacy.

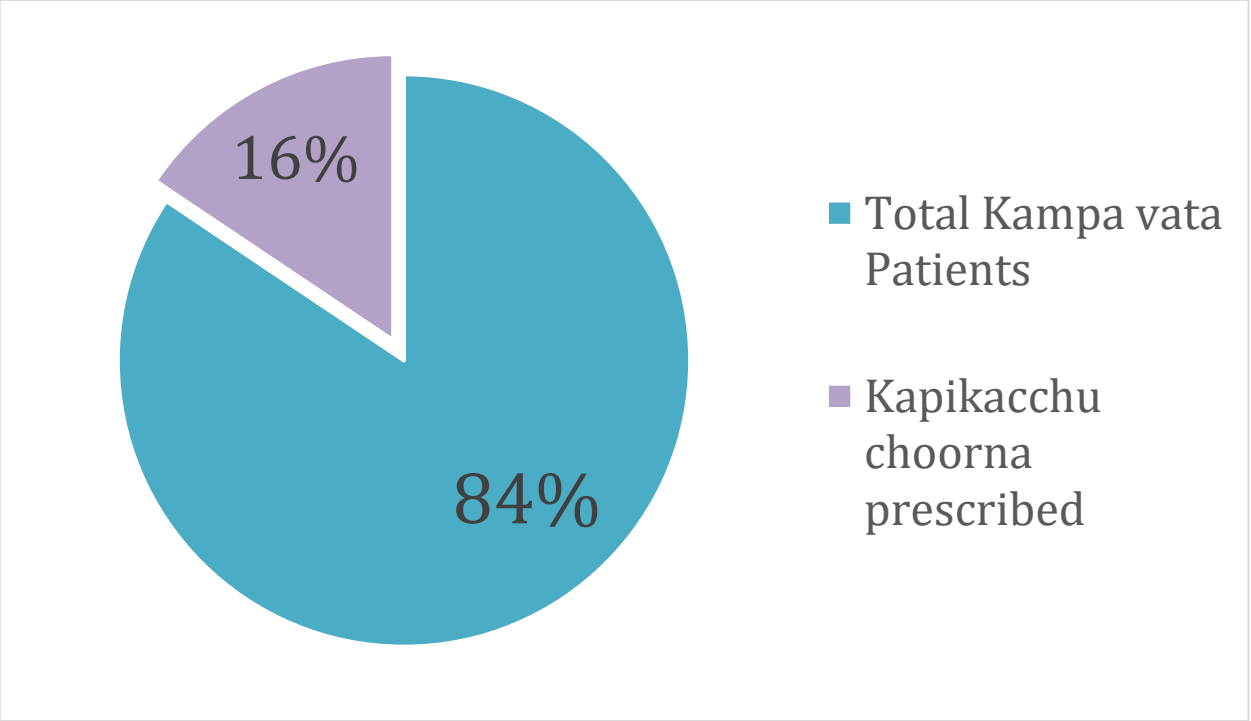


Figure 3.13 – Percentage of *Kapikacchu choorna* prescription in *Kampa vata* patients

CONCLUSION

Kapikacchu, along with its synonyms, is not mentioned in the Vedic period, indicating that this drug received no references during that time. Plant names in ayurvedic texts have several synonyms. Here a brief attempt was made to trace the synonym usage for *Mucuna pruriens (L.) DC* (MP), which today is more popularly called *Kapikacchu*. MP has more than 25 synonyms associated with it. Of these *Kapikacchu* is not mentioned in the Sushruta Samhitha and the Sutrasthana's of Caraka and Ashtanga Hridaya. A synonym that occurs across brihat trayees is *Atmagupta*. The ayurvedic properties of MP across the classical literature are *Vatahara and Brumhana,* with it's use as *Vajikara* drug being the most common.

The retrospective analysis reveals that in contemporary Ayurvedic practices, of those prescribed *Kapikacchu choorna* (MP), approximately 40% are for patients with *Kampa Vata*. Interestingly, among patients diagnosed with *Kampa Vata*, a condition analogous to Parkinson's disease, only 16% are prescribed *Kapikacchu choorna*.

Long-term feeding of MP influences lipid metabolism in wild-type (*CS*) flies, aligning with its *Brumhana* (nourishing) property as described in Ayurvedic texts. However, short-term feeding experiments on both *park*^{13} mutant and wild-type flies revealed no significant change in triacylglycerol (TAG) levels. Fecundity was unaffected by *Kapikacchu* and this may be a reflection of its property to increase libido rather than fertilisation. It was also observed that *CS* flies treated MP demonstrated enhanced resistance to oxidative stress compared to normal diet fed flies, suggesting significant neuroprotective activity. This indicates that *Kapikacchu* may offer protective benefits against cellular damage induced by oxidative stress, potentially contributing to its therapeutic effects in neurodegenerative conditions such as Parkinson's disease.

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APPENDIX

Study Protocol

Institutional Ethics Committee for Human Research

Application for Ethical Review of Research Protocol

To

Date:25-05-2024

The Member Secretary

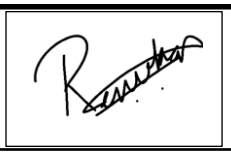
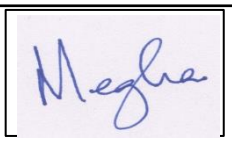
Institutional Ethics Committee

The University of Trans-Disciplinary Health Sciences and Technology

Bengaluru

Full name of Principal Investigator:	RENUKA A
Designation:	Internee- 2nd year MSc Life Sciences (AB)
Complete Postal Address:	The University of Trans-Disciplinary Health Sciences and Technology; # 74/2, Jarakabande Kaval, Attur post, Via Yelahanka, Bengaluru – 560064, Karnataka
Tel. No: Office / Mobile	8129946460
E-mail ID:	renuka.a@tdu.edu.in

Site of study:	IAIM Health Care Centre, #74/2, Jarakabande Kaval, Post Attur via Yelahanka, Bangalore - 64
Title of Project:	**Exploring the Clinical Application of *Kapikacchu* (Mucuna Pruriens) with special reference to Parkinson's Disease: A Retrospective Study**
Sponsor Name and address:	Not Applicable (self funded).

Sl. No.	**Name**	**Signature**
Principal Investigator	Renuka A	
Guide	Dr Prasan Shankar	
Co-Guide	Dr Megha	

Type of study: Local / National / International	Local
Type of Trial: Multi centre / Single centre	Single centre
Collaborative study: Yes / No If Yes, Name the Collaborative Institutes:	No

Renuka A

Name & Signature of Principal Investigator **Date:** 25-05-2024

Protocol Cover Page

Title of the Protocol: Exploring the Clinical Application of *Kapikacchu* (Mucuna Pruriens) with special reference to Parkinson's Disease: A Retrospective Study.

PROTOCOL NUMBER: TDU/IEC/15/2024/PR60

PROTOCOL VERSION & DATE: 1.3 dated: 25 May 2024
1.4 dated: 12 June 2024
1.5 dated: 18 June 2024

GENERAL INFORMATION

1. **Name and title of the investigator(s) and supervisor responsible for the study with address and phone number(s):**

1. **Dr. RENUKA A - PRINCIPAL INVESTIGATOR**
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2. **Dr. PRASAN SHANKAR - GUIDE**
   IAIM Healthcare Centre

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3. **Dr. MEGHA - CO- GUIDE**
   Associate Professor,

   Centre For Ayurveda Biology and Holistic Nutrition

   TDU, #74/2, Jarakabande Kaval, Attur post, Via Yelahanka, Bengaluru – 560064, Karnataka

2. **Roles and responsibilities of the investigators:**

Sl. No.	**Name**	**Roles (PI/Co-I/A advisor**	**Responsibilities in the project**
1.	Dr. Renuka A	PI	● Develop a process for data collection ● Collate data for analysis ● Analyse data ● Write manuscript
2.	Dr. Prasan Shankar	Guide	● Supervise process development ● Guide to analyse data ● Guide to write the manuscript
3.	Dr. Megha	Co- Guide	● Supervise process development ● Guide to analyse data ● Guide to write the Manuscript

3. Authority to sign the protocol and amendments

Name & Designation	Affiliation, Address and Phone number
Dr. PRASAN SHANKAR Medical Director, I-AIM	IAIM Healthcare Centre, #74/2, Jarakabande Kaval, Attur post, Via Yelahanka, Bengaluru – 560064, Karnataka Ph: 9945426118

2) Details of the study monitor (if applicable): NA

3) Details of the medical expert for the study (if applicable): Dr Prasan Shankar

4) Details of the clinical laboratories and/or other collaborative institutions involved in the study / trial (if applicable): NA

5) Details of the study sponsor: NA

Table of Contents

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GENERAL INFORMATION

Table of Contents

List of Abbreviations

MP- Mucuna Pruriens

PD- Parkinson's disease

API- Ayurvedic Pharmacopoeia of India

EMR- Electronic medical record

L-Dopa- Levodopa

HMIS- Health Management Information System

MR number- Medical record number

MS Excel- Microsoft Excel

I-AIM- Institute of Ayurveda and Integrative Medicine

1) Introduction and Background

Kapikacchu (*Mucuna pruriens*), colloquially known as velvet bean, boasts widespread distribution across tropical and subtropical regions globally. Revered for its medicinal efficacy, *Kapikacchu* has long held prominence in traditional practices and within the realms of Indian systems of medicine. Originating from China and India, *Mucuna pruriens* (MP) is an annual climbing legume characterised by its hairy, robust, and leathery pods, measuring approximately four inches in length. Diverse communities worldwide incorporate its seeds into their consumption patterns (1).

In the annals of Ayurveda, *Kapikacchu* finds mention dating back to the samhitha period (1500 BCE – Seventh century), where it is documented as a remedy for *vajikarana chikitsa (*~Aphrodisiac*)*(11), *vatavyadhis*(diseases caused due to the vitiation of vata)(11), and various other conditions related with *raktha*(~blood), often as an integral component of distinct formulations like vidaryadigana(12). In nighantus, such as Bhavaprakasha nighantu, the seed of *Kapikacchu* is specifically noted for its vatashamana(vata dosha pacifying) and vajikarana (~aphrodisiac) properties(13). As per the Ayurveda Pharmacopoeia of India (API), MP seeds embody therapeutic attributes such as *Tridoshahara* (pacify all three doshas) , *Vrushya* (~aphrodisiac), *Raktadoshanashaka* (~pacify blood related disorders), *Brumhana* (~nourishing), *and Balya* (~improves strength). Major chemical constituents found are Fixed Oil, Alkaloid and 3,4-Dihydroxyphenylalanine. Recommended dosages ranging from 3 to 6 grams are said to be efficacious in addressing ailments including *Vatavyadhi, Kampavata, Klaibya, Raktapitta, Dushtavrana, and Daurbalya* (2). In modern medicine these conditions can be correlated with: neurological disorders, Parkinson's disease, infertility, movement disorders, bleeding disorders and Chronic ulcers. The Ayurvedic literature references *Kapikacchu* through over 25 synonyms, reflective of its diverse morphological and functional aspects, as elucidated in texts like Kaiyadeva nighantu and bhavaprakasha nighantu.

A review by Pathania et al., underscore the therapeutic potentials of MP, spanning from its efficacy against snake poisoning to antimicrobial, anti-epileptic, neuroprotective, aphrodisiac, and antioxidant activities (3). Contemporary medical practices witness the utilisation of Mucuna seed preparations in Parkinson's disease (PD) management, given their natural source of L-Dopa (Levodopa) (3–10). L-Dopa is the precursor of Dopamine- a neurotransmitter widely used in the treatment of Parkinson's disease. Certain reports propose that its effect on PD is due to the antioxidant property along with the presence of L-Dopa (4,5).

Ayurvedic physicians advocate for the integration of *Kapikacchu* in PD symptomatology management and several studies have demonstrated its significant effects on the condition(14–16) being a potent vata pacifying drug. Kampa vata(a condition having strong clinical corelation with Parkinson’s disease), a disease caused by the vitiation of vata as mentioned in Basavarajiyam, has long been treated in Ayurveda using *Kapikacchu* and its preparations(Katzenschlage, mali, Dharmani)(4,5,7). Numerous studies have demonstrated a significant reduction in Parkinson's disease symptoms with the administration of *Kapikacchu*. Though *Kapikacchu* is indicated for various ailments classically as outlined in annexure 1, this study endeavours to investigate the patterns of *Kapikacchu* utilisation in the real-world scenario among the Ayurvedic Physicians by analysing the prescriptions that include *Kapikacchu*, with a particular focus on its use for Parkinson’s disease(*Kampa vata*). For this, taking the example of I-AIM Healthcare Centre (The Institute of Ayurveda and Integrative Medicine) - a high quality 100 bed, integrative healthcare hospital, which was established in 2011. After consulting with

doctors and gathering information, it became evident that *Kapikacchu* Choorna is primarily prescribed for Kampa vata (~Parkinson's disease), along with other indications and uses. By reviewing the medical records of the past five years in the IAIM hospital, this study is expected to understand the current usage status of *Kapikacchu* among the Ayurveda physicians either as a single drug or as a formulation with a particular emphasis on Parkinson's disease.

Moreover, a comprehensive review of classical literature on *Kapikacchu* will be conducted to understand its various classically mentioned applications. Additionally, a laboratory-based investigation will be undertaken to elucidate the metabolic effects of *Kapikacchu*, utilizing both wild type and Parkinson's disease model in *Drosophila melanogaster*.

Most common formulations having *Kapikacchu* as a main ingredient used in IAIM Healthcare Centre-

Classical;

1) *Kapikacchu choornam*

Proprietary;

1) *Geriforte tab*
2) *Ashwagandhadi leham*
3) *Ashwamed capsule*
4) *Neo tab*
5) *Shilapravang*

2) Study Objectives

1. To review the practical utilisation of *Kapikacchu* in contemporary ayurvedic practice, over the past 5 years in IAIM Health care centre.
    - To review the specific implementation of *Kapikacchu* in Kampa vata(Parkinson's disease).

3) Methodology

3.1) Study Design/Type

Retrospective chart review:

1. Review the last 5 years (Jan 2019 - Dec 2023) patient's database of IAIM Healthcare Centre using EMR (Electronic Medical Record).
2. Filter for those who have prescribed with *Kapikacchu* either singly or in a formulation with special emphasis on PD.
3. Filter those who are diagnosed with 'Vatavyadhi-Kampa' using the code- V2.34.0
4. Record the anonymized data (annexure 2) of the patients filtered above.
5. Cross checking the data manually with the MR numbers.

6. Classify the diseases into ICDS-11 form and tabulate associations between disease class and prescriptions.
7. Visualising the data using Microsoft excel 2019 (Version 2402).

- Descriptive statistics
- Visualisation tools

3.2) **Study Duration:** 4 months

3.3) **Study location:** I-AIM Healthcare Centre

3.4) **Primary outcome measures:**

- List of clinical conditions where *Kapikacchu* (as a single drug or in formulation) is prescribed at IAIM Healthcare Centre.
- Percentage of usage of *Kapikacchu* on different clinical conditions.
- Descriptive statistics of *Kapikacchu* usage (as a single drug or in formulation) at IAIM Healthcare Centre.

3.5) **Secondary outcome measures:**

- Report on analysis of *Kapikacchu* usage in Parkinson's disease management at IAIM Healthcare Centre.
- Percentage and descriptive statistics of *Kapikacchu* and its preperations prescribed for Parkinson's disease management.

4) Selection of Subjects

4.1) Inclusion Criteria:

- Patients of all age and gender who consulted IAIM Healthcare Centre (inpatient or outpatient), and having prescription of *Kapikacchu*: as a single drug or as a formulation and have purchased medicine from IAIM pharmacy.

- Patients who had consulted and purchased medicine from January 2019 to December 2023.

- Patients who are diagnosed as 'Vatavyadhi- kampa'.

4.2) Exclusion Criteria

- Any record with incomplete symptomatic description or unclear disease class.

5) Withdrawal of Subjects: NA

6) Proposed Intervention: NA

7) Data Collection Procedures, Instruments Used, and Data Quality Control

7.1) Data collection tools & Data collection procedures:

Data collection tool: Electronic Health Records of IAIM Healthcare Centre (from the Health Management Information System (HMIS)).

Data collection procedure:

- With the permission of the hospital in charge/ director, anonymized data of patients will be collected from the pharmacy, with MR numbers (Medical record numbers).
- The MR numbers of patients who have purchased the list of formulations mentioned in the introduction part will be sought from the pharmacy.
- Filter for those who have prescribed with *Kapikacchu* and its preperations.
- Filter those who are diagnosed with 'Vatavyadhi-Kampa' using the code- V2.34.0
- From the EMR system, by using MR numbers collect the details of demographic data, clinical history, examination, lab investigations, comorbidities, medication history and diagnosis will be collected using the MR numbers.
- Review the data using MS Excel 2019 (Version 2402) – descriptive statistics and visualisation tools.

8) Assessment of Efficacy: NA

9)Ethical considerations:

- All data will be anonymouslyAnonymized data will be collected and data visualisation will be conducted in a manner that encompasses comprehensive data analysis, drawing conclusions from the dataset as a whole. This ensures that individual patient data cannot be traced back to an MR number.
- Before the commencement of the study, approval for the study protocol will be sought from the Institutional Ethics Committee (IEC).

10) Statistical Plan

10.1) Statistical Methods and Models of Data Analysis

Descriptive statistics of usage of *Kapikacchu* over a period of 5 years and data visualisation using MS excel 2019 (Version 2402).

10.2) Subject Population(s) for Analysis

- Patients of IAIM Healthcare Centre, who are prescribed with *Kapikacchu* in any form.
- Patients of IAIM Healthcare Centre, who report Parkinson's disease or Parkinson's-like symptoms.

11) Finance and Insurance: NA

12) Publication Plan

The study will be published in M.Sc. Project Dissertation and if significant, will be considered for publication in a peer-reviewed journal.

13) REFERENCES

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3. Pathania R, Chawla P, Khan H, Kaushik R, Khan MA. An assessment of potential nutritive and medicinal properties of Mucuna pruriens: a natural food legume. 3 Biotech. 2020 Jun;10(6):261.
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5. Rai SN, Chaturvedi VK, Singh P, Singh BK, Singh MP. Mucuna pruriens in Parkinson's and in some other diseases: recent advancement and future prospective. 3 Biotech. 2020 Dec;10(12):522.
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Stizolamine, and Some Fructooligosaccharides. Compounds. 2022 Dec 27;3(1):1–16.

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SUPPLEMENTS

ANNEXURE 1- *Rasapanchaka* and *Phalasruthi* of *Kapikacchu* (according to API)

Rasapanchaka	*Phalasruthi*
Rasa : Madhura, Kasaya *Guna : Guru, Snigdha* *Virya : Sita* *Vipaka : Madhura*	*Kaphanashaka, Vatasamana, Vrishya, Pittanashaka, Rakthadoshanashaka, Brumhana, Balya*

ANNEXURE 2- Required details from the HMIS

Sl.no	**Details of data from HMIS**
1)	MR.NO
2)	Personal/Demographic data – Age, Sex, Nationality
3)	Department in which the patient has consulted
4)	Chief complaint
5)	History of presenting complaints
6)	Past/Family/Personal history – Medical history, Family history, Drug history, Diagnostic history
7)	Consultation details- Roga vinischaya, Allopathic diagnosis, Diagnostic type, Description
8)	Investigations
9)	Prescription details

ANNEXURE 3– CV OF INVESTIGATORS

1) CV of PI

Personal information

Dr. Renuka A

BAMS,

2nd year MSc Life sciences (AB)

The University of Trans-Disciplinary Health Sciences and Technology (TDU), Bengaluru

Phone: 8129946460

E-mail: renuka.a@tdu.edu.in

Education

- MSc . LIFE SCIENCES (AYURVEDA BIOLOGY)

The Institute of Transdisciplinary Health and Technology, Bangalore

2022- Present

- CERTIFICATE COURSE IN MARMA CHIKITSA

National Ayurveda Research Institute for Panchakarma, Kerala

2022

- CERTIFICATE COURSE IN COSMETOLOGY AND TRICHOLOGY IN AYURVEDA

PAMPA Mstery programme

2020

- BACHELOR OF AYURVEDIC MEDICINE AND SURGERY

Santhigiri Ayurveda Medical College

2020

Experience

- Physician

Vaidhyaraj Ayurveda Meenakshipuram, Tamil Nadu

May 2022 - September 2022

- Physician

Satwikam Ayurveda Vaidyasala, Palakkad, Kerala

April 2022 - September 2022

- Self Employed

2020-2022

- Training

Ayurveda Health Care centre and Research Institute

Under the guidance of Dr N V Sreevaths and Dr Arathi P S

October - December 2018

Internship

- Govt Ayurveda dispensary, Perumatty,

Under the guidance of Dr Raja Hariprasad

3 months, 2019

- National Ayurveda Research Institute for Panchakarma, Cheruthuruthy, Kerala

1 month, 2019

- Rotatory Compulsory Internship

Santhigiri Ayurveda Medical College, Palakkad.

8 months, 2019- 2020

Activities

- Undergone service in Task force group for CoVID-19 prophylactic project conducted by National Ayurveda Research Institute for Panchakarma, Cheruthuruthy.
- Conducted and participated in various health camps and medical check ups in Palakkad.

Paper presentations

- Presented a paper on the topic Adulteration of food and its side effects at Amrutam2017- National workshop at Santhigiri Ayurveda Medical College.
- Presented a paper on the topic Shatadhauta ghruta in various diseases at Samavarthana 2017 - National Symposium at Vaidyaratnam P.S. Varier Ayurveda college, Kottakkal

2) CV of Guide

Curriculum Vitae
Personal Information

Dr. Prasan Shankar
B.A.M.S, M.D Ayurveda
Medical Director
I-AIM Healthcare Centre, Bangalore

Address:
#74/2, Jarakabande Kaval, Post Attur via Yelahanka, Bangalore. PIN: 560 064, Telephone Number(s): 080-28567000, +919945426118(Cell), Fax: 080 28567926,

E-mail:

prasan.shankar@iaimhealthcare.org

Brief Background:

Dr. Prasan Shankar is an Āyurveda Physician working in the Rasayana tantra (Geriatric) unit at the Institute of Āyurveda and Integrative medicine (I-AIM)-TDU. He treats various neurological and neurodegenerative disorders like strokes and parkinsonism, arthritis spectrum disorders, supportive and complementary cancer care, supportive cardiac care and other age related problems. He has an interest in doing research around practice and is involved in research related to Āyurvedic management of neurological disorders, cancer and is currently involved in various research projects. Integrative healthcare, Rasayana or Rejuvinative medicines/ practices in Ayurveda, Pratice based evidence, Clinical Research, Research in neurological disorders, complimentary cancer care,

He has an M.D in Pañcakarma from Rajiv Gandhi University of Health Sciences, Bangalore. He is currently the Medical director at Institute of Āyurveda and Integrative medicine(I-AIM)-TDU.

Professional Interest:

Ayurveda Physician, Ayurveda Biology, Clinical Research

3) CV of Co-Guide

Megha Ph. D.
The University of Trans-Disciplinary Health Sciences and Technology (TDU),
Bengaluru megha@tdu.edu.in; +91 7259491805

2006 Ph.D. *Biochemistry and Structural Biology*
Stony Brook University, New York

2022 ePG Diploma Public Health Nutrition (Course grade: A)
PHFI, New Delhi

Work Experience

Jan 2020 - present *Associate Professor, TDU*

July 2019 - Dec 2020 *Assistant Professor,*
Centre for Ayurveda Biology and Holistic Nutrition
TDU, Bengaluru

Mar 2012 - June 2019 *Postdoctoral Fellow,*
Wellcome Trust/ DBT India Alliance Early Career Fellow
National Center for Biological Sciences (TIFR), Bengaluru

Dec 2009 - Jan 2012 *Grants and Programme Manager*
The Wellcome Trust/ DBT India Alliance, Hyderabad

Jan 2009 – Nov 2009 *Grants Adviser*
The Wellcome Trust/ DBT India Alliance, Hyderabad

May 2006 – Aug 2008 *Senior Fellow*
University of Washington, Seattle

Research Experience

Centre for Ayurveda Biology and Holistic Nutrition, TDU, Bengaluru We aim to tackle malnutrition through traditional foods and dietary concepts by seeking convergence through two different angles: mechanistic studies using *Drosophila melanogaster* and public health nutrition.

We have developed an early life malnutrition model in flies where we study how nutritional stress during development impacts adult gut physiology and function. Further, this model is used for interrogating health benefits of food ingredients such as amla, rice and jackfruit. Through a documentation project on "Traditional Foods of Karnataka" we are compiling traditional knowledge on food dishes and deconstructing them through a nutritional and ayurvedic lens.

In an observational study on cancer patients, we are designing diets that combine IDA recommendations and ayurvedic principles, with a goal to assessing their impact on patient wellbeing.

National Centre for Biological Sciences (TIFR), Bengaluru *Prof. Gaiti Hasan's lab*
Intracellular Ca^{2+} signaling, *Drosophila melanogaster,* neuropeptide-producing cells, early life nutrition

University of Würzburg, Germany *Collaborative visit, July 2014- September 2014, Prof. Dr. Christian Wegener's Lab*
Semi-quantitation of neuropeptides via mass spectrometry.

University of Washington, Seattle, USA *Senior Fellow, May 2006 – Aug 2008, Prof. Samuel I Miller's lab*
Functional characterization of a *Salmonella typhimurium* effector protein, *SseJ*.

State University of New York, Stony Brook, USA
PhD Student, August 2001 - March 2006 , Prof. Erwin London's lab
Investigated the structural role of ceramide and cholesterol in the formation, and stability of lipid rafts using fluorescence spectroscopy. Found ceramide could displace cholesterol from lipid rafts, and both sterol structure as well as ceramide structure (can influence this property. Piloted the development of asymmetrical lipid vesicles.

Funding
- "Traditional foods of Karnataka - a nutritional and ayurvedic perspective" (~ INR 45 Lakhs; 2023-25; AYUSH-CCRAS)
- Darshan Shankar Amla Fellowship [~INR 6.5 Lakhs; 2022-2024, Internal TDU] - Start up Research Award (~INR 30 Lakhs; 2020 - 2022; DST-SERB) - Sentinel Award (INR 36.07 Lakhs; 2019-2021; Bill and Melinda Gates Foundation via BIRAC)
- Early Career Fellowship (INR 1.46 Cr; 2013-2019; The Wellcome Trust/ DBT India Alliance)

Teaching Experience
- Biochemistry (4 credits), Animal physiology (1 credits), Biochemistry and Molecular Biology Lab (2 credits) and Communicating Research (1 credit) for MSc Life Sciences (Ayurveda Biology) Students.
- Ayurveda Dietetics courses: Online & offline (1 - 3 credits)
- Developed and taught a 4 hr Nutrition module for School Children: Classes 5, 6 & 7. - 8-week certificate course for BSc/ MSc level students: 2017, 2015, 2014 - 2-month summer course for interns at NCBS: 2013

Non-research Work Experience

(2020 - present) Co-coordinating the design and implementation of a unique 2 year MSc program called M.Sc. Life Sciences (Ayurveda Biology).

(2020 - present) Coordinating and teaching in an innovative program in nutrition science: Ayurveda Dietetics.

(2019) Selected for and completed a 4-day workshop "Understanding Public Health Nutrition: towards policy and action". Delivered by PHFI, New Delhi and IFPRI, New Delhi. (2019) Completed a 5-day workshop on Evidence-based Science Policy making by IISER Pune, British Council. Delivered by Dialogue Matters, UK

(2018) Policy work on student aspiration in STEM. Collaborative project with Dr Shambhavi Naik, Takshashila.

(2018) Completed a 4-week course by Takshashila Institute on Science, Technology

and Policy
(2018) Organised a two day teacher-training program for Agastya Foundation biology and chemistry teachers, November 2018
(2013-2016) Founder-member and built-up the Postdoc Association at NCBS. (2009-2012) The Wellcome Trust/DBT India Alliance (IA) is independent non-profit jointly funded by The Wellcome Trust, UK and Department of Biotechnology, Government of India.

Conferences (last 5 years)

2023 EMBO Workshop: Developmental metabolism: flows of energy, matter, and information [Virtual]
2022 Indian NeuroBehaviour Conference (Talk)
2021 Indian Drosophila Research Conference, virtual (Poster)
2020 Keystone eSymposia: Optimizing Nutrition for Maternal, Newborn and Child Health
2020 Asia-Pacific Drosophila Research Conference, Pune (poster)
2019 Understanding Public Health Nutrition: towards policy and action **2018** Indian Society for Developmental Biology Biennial Meeting, Kanpur (poster, talk declined)
2017 3rd International Insect Hormone Workshop, Japan (talk)
2017 Indian Society for Developmental Biology Biennial Meeting, Pune (poster+talk) **2017** Young Investigator's Meeting, Goa (poster + talk)

Publications

1. *Breaking silos: can the emerging field of Ayurvedic biology contribute to the advancement of Indian health science*
   Bhavya Vijay, Gurmeet Singh, Chethala N. Vishnuprasad, Ashwini Godbole, Subrahmanya Kumar Kukkupuni, Megha, Prasan Shankar, Poornima Devkumar and Darshan Shankar **Current Science 2022; 122(3): 251-257**
2. *Impact of late larval nutritional stress on adult metabolic, gut and locomotor phenotypes in Drosophila melanogaster*
   Shri Gouri Patil, Sushmitha Sekhar, Aman Agarwal, TS Oviya, Debashis Rout, **Megha bioRxiv 2022.06.30.498321; doi: https://doi.org/10.1101/2022.06.30.498321** *3. Surviving nutritional deprivation during development: neuronal intracellular calcium signaling is critical*
   Megha, Gaiti Hasan. Int. J. Dev. Biol. 2020 64: 239 - 246
4. *Neuropeptides required for Drosophila development under nutritional stress are regulated by the ER-Ca2+ sensor STIM*
   Megha*, Christian Wegener and Gaiti Hasan. PLoS One. 2019 Jul 11;14(7):e0219719. *Corresponding author.
5. *Control of protein translation by IP_3R-mediated Ca^{2+} release in Drosophila neuroendocrine cells.*

Megha and Gaiti Hasan, Fly, 2017, 11:4;290-296

6. *IP_3R mediated Ca2+ release regulates protein metabolism in Drosophila neuroendocrine cells: implications for development under nutrient stress*
Megha and Gaiti Hasan, Development 2017 Apr 15;144(8):1484-1489 (Media coverage in The Hindu and //thewire.in)

7. *Metabolic labelling to quantify Drosophila neuropeptides and peptide hormones.* Kunz T, Chen J, **Megha**, Wegener C.
Book Chapter in *Peptidomics: Methods and Protocol*
2018;1719:175-185. *8. Activation of a bacterial virulence protein by the GTPase RhoA.*
Christen M, Coye LH, Hontz JS, LaRock DL, Pfuetzner RA, **Megha**, Miller SI. Sci Signal. 2009;2(95):ra71 (Selected by Faculty 1000)

9. *Preparation and properties of asymmetric vesicles that mimic cell membranes: effect upon lipid raft formation and transmembrane helix orientation.*
Cheng HT, **Megha**, London E. J Biol Chem. 2009;284(10):6079-92. (US Patent filed based on this work and Selected by Faculty 1000)

10. *Effect of ceramide N-acyl chain and polar headgroup structure on the properties of ordered lipid domains (lipid rafts).*
Megha, Sawatzki P, Kolter T, Bittman R, London E. Biochim Biophys Acta. 2007;176 8(9):2205-12.

11. *Cholesterol precursors stabilize ordinary and ceramide-rich ordered lipid domains (lipid rafts) to different degrees. Implications for the Bloch hypothesis and sterol biosynthesis disorders.*
Megha, Bakht O, London E. J Biol Chem. 2006 4;281(31):21903-13.

12. *Relationship between sterol/steroid structure and participation in ordered lipid domains (lipid rafts): implications for lipid raft structure and function.*
Wang J, **Megha,** London E. Biochemistry. 2004 3;43(4):1010-8.

13. *Ceramide selectively displaces cholesterol from ordered lipid domains (rafts): implications for lipid raft structure and function.*
Megha, London E. J Biol Chem. 2004 Mar 12;279(11):9997-10004. (Selected by Faculty 1000)

PROGRESS REPORT 1

KAPIKACCHU - CLINICAL RETROSPECTIVE AND DROSOPHILA STUDIES

OBJECTIVES;

- Review of classical literature on the properties and suggested use of Kapikacchu - using TDU database and other resources.
- Retrospective on Kapikacchu use at IAIM - using IAIM data to understand how clinicians are prescribing Kapikacchu, singly or in formulation, and for what condition. Also to reflect on the findings in the context of #1. ie., what is the contemporary use of Kapikacchu?
- Lab based investigation on the metabolic effects of Kapikacchu - in healthy and diseased (Parkinson's) flies (Drosophila melanogaster).

PROGRESS MADE;

- On the first objective, I have collected data from different samhitha's and nighantus (not complete) and are arranging them into an excel file.
- Have talked with experts in this field and are getting ideas on what basis to collect and arrange the literature part.
- On the second objective; though I have got some of the data regarding the use of Kapikacchu by the physicians and was able to assess the hospital system for the same, I am in the process of getting ethical clearance to do the retrospective study.
- I have talked with the expertise in this area, and the work is in progress.
- On the third objective; I'am doing the maintenance of PARK13 and CS flies.
- Practicing the BCA and TAG assays and doing the preparatory works.
- Studied to prepare the normal standard diet for the flies.
- Sorting the flies into male and female using carbon dioxide and ice.
- In the process of studying Kapikacchu media preparation.

SKILLS LEARNED;

- Maintenance of flies.
- Flipping of the flies.
- Sorting them to males and females.
- Their normal media preparation.
- To do BCA and TAG assay.
- To use Spectrophotometer, centrifuge, and incubator for the assays.
- To talk, a little bit.

CHALLENGES FACED;

- To mingle and talk with different people.
- Doing calculations for the assays and other processes.
- Studying, understanding and processing the new knowledge.
- Getting mentally organized with the objectives and day-to-day activities.
- Managing the timing and switching to different objectives in a day is a challenge.
- To elaborate on the protocol for ethical clearance.

PROGRESS REPORT 2

KAPIKACCHU - CLINICAL RETROSPECTIVE AND DROSOPHILA STUDIES

PROGRESS MADE ON OBJECTIVES;

- Collected data from brihat trayee on Kapikacchu.
- Data have been seggregated on the basis of the repetation of synonyms.
- On the third objective i have started experiments with *Park 13/*+ flies.
- Fecundity, TAG, and BCA experiments with both *Park 13/*+ and *CS* flies are progressing.
- For this I've studied to set up the cross to get a heterozygous population, maintaining a cross and collection of virgins.
- Also did larval collection.
- Media preperation with *Kapikacchu choorna* on different doses.

SKILLS LEARNED;

- Planning of experiments
- Time management
- Presentation skills
- Virgin collection of both *Park 13/ tb* and *CS* flies.
- Larval collection of both *Park 13/*+ and *CS* flies.
- Setting up a cross and producing heterozygous population.
- Medicine media preperation.
- To check Fecundity.
- Using a microscope.

CHALLENGES FACED;

- Time management
- Planning and organizing the assays and day-to-day work.
- Switching from research in lab to clinical retrospective.

PROGRESS REPORT 3

KAPIKACCHU - CLINICAL RETROSPECTIVE AND DROSOPHILA STUDIES

1. Review of classical literature on the properties and suggested uses of Kapikacchu.
2. Retrospective on Kapikachhu use at IAIM. - Using IAIM data to understand how clinicians are prescribing Kapikachhu, singly or in formulation, and for what conditions.
3. Lab-based investigation of the metabolic effects of Kapikacchu (*Mucuna pruriens*) - in healthy and diseased (parkinson's) flies.

Progress made;

- Done 3 trails of TAG and BCA assay on both *Park 13*/+ and *CS* flies with two different doses of feeding.
- Two trials of the fecundity experiment are finished and the third one is in progress.
- Study protocol for ethics committee approval is submitted to IEC.
- Data collection from the hospital is progressing.

Skills learned;

- Planning of experiments.
- Time management
- Presentation skills
- Virgin collection of both Park 13/ tb and CS flies.
- Larval collection of both Park 13/+ and CS flies.
- Setting up a cross and producing a heterozygous population.
- Medicine media preparation.
- Fecundity experiment.
- Using a microscope.
- Analyze data with MS excel.
- Usage of prism graph pad.
- Writing a study protocol.

Challenges faced;

- Time management
- Planning and organizing the assays and day-to-day work.
- To analyze the data.