

Effects of *Bacopa monnieri* herbal supplement on aging and neurocognitive functions with relation to constitution (*Prakriti*) in healthy adults. Clinical trial protocol

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Abstract

Background: Aging is an irreversible process influenced by both internal (genetic) and external (environmental) factors. These factors contribute to differences in how individuals age. Aging is not just about a decline in physical and mental abilities but involves complex biological mechanisms. Two main theories explain aging: 1. Programmed Theories: Suggest that aging follows a biological clock; and 2. Error Theories Propose that aging is caused by environmental damage to cells, leading to DNA damage and the accumulation of harmful substances. Telomere shortening is a major contributing element to aging. With every cell division, the protecting telomeres at the ends of chromosomes get shorter. When they become too short, cells stop dividing, a process known as cellular senescence. Telomere length is maintained by an enzyme called telomerase, but its activity decreases with age. Aging is also associated with changes in the brain, including a decline in cognitive abilities like memory and decision-making. These changes can be observed through brain activity using techniques like EEG (electroencephalography). This study aims to explore whether an *Bacopa monerri* freeze dried herbal decoction can help slow aging-related changes, maintain telomere length, and improve cognitive functions.

Study design: This is a two-arm, open-label, non-inferiority, randomized controlled clinical trial enrolling participants (The MoCA score of 24 or above). This study aims to assess the potential of BMFD-*Bacopa monerri* freeze-dried decoction -the interventional dosage) in stabilizing the aging process and influencing cognitive functions in the elderly Participants. Participants will be allocated randomly into the two arms and consider testing dosage form (BMFD), which has the highest anti-aging activity and the highest anti-lipase activity and placebo to evaluate if the BMFD dosage form is better at stabilizing the process of aging and aging-related neurocognitive functions as compared to placebo. The duration of the BMFD dosage form or placebo administration will be 45 days. It will be given as 120 ML twice a day. They will be requested to take a daily dose of 120 ml of BMFD twice a day before meals. The total duration of BMFD administration is 45 days. The follow-up duration for this study is set to 45 days. Participants will be recruited from a single-center clinical trial at the Clinical Trial Center, Faculty of Indigenous Medicine, University of Colombo, Sri Lanka. The study aims to evaluate the effects of BMFD decoction on neurocognitive functions and aging-related changes in the elderly. The primary outcomes will be assessed at baseline, 45 days, and 90 days. These include: neurocognitive functions, measured using the Montreal Cognitive Assessment (MoCA) validated for the Sri Lankan population. telomerase activity and telomere length of blood mononuclear cells, assessed using qualitative polymerase chain reaction (QPCR). Peripheral nerve conduction: Upper limbs -Median nerve and Ulnar nerve and lower limbs: Tibial and Common peroneal nerve, assessed using the nerve conduction test (NCT). Electrical activity of the brain, measured through electroencephalography (EEG). Secondary outcomes include the assessment of Health-Related Quality of Life (HRQoL) using a HRQoL questionnaire (Janković, Slobodan M., et al., 2021), evaluated at baseline, 45 days, and 90 days. This trial utilizes a product (BMFD decoction) already tested for efficacy in other contexts, ensuring its safety for use in this population. The outcomes will provide valuable insights into how BMFD can stabilize neurocognitive functions and aging-related changes, enabling early interventions and personalized preventive strategies.

Discussion: This clinical trial will provide evidence-based scientific data on the effectiveness of *Bacopa monnieri* and its Ayurvedic dosage form, BMFD, in the aging process and neurocognitive enhancement concerning individual constitution (*Prakriti*). This trial is expected to contribute to the early detection of cognitive impairment and aging-related neurophysiological changes in relation to individual constitution (*Prakriti*).

Trial registration: ISRCTN64126920 <https://doi.org/10.1186/ISRCTN64126920>

Background

Aging: A Multifactorial and Irreversible Process;

Aging is an irreversible, multifactorial process influenced by both intrinsic (genetic) and extrinsic (environmental) factors. These factors contribute to the diversity observed in aging, with longevity largely determined by an individual's genetic makeup and their surrounding environment. Aging is not simply a decline in bodily functions, but rather a complex, multifactorial mechanism [1, 2]. The decline caused by aging can be categorized into two main theories: the programmed theories, which suggest aging is regulated by biological clocks, and the error theories, which propose that environmental factors lead to a gradual accumulation of DNA damage, free radicals, and macromolecular cross-linking [2]. Aging has also been linked to cellular senescence, which results from telomere shortening (replicative senescence) or cell stress (cellular senescence) [2].

The Role of Telomeres in Aging;

Telomeres are specialized structures at the ends of chromosomes, made up of clusters of G residues [3]. They play a crucial role in maintaining chromosomal stability by ensuring complete replication of chromosomal DNA during cell division [4]. However, telomeres shorten with each cell division, leading to replicative senescence. When telomeres become critically short, the chromosome's ends degrade, causing progressive loss of genetic material. Telomerase, a specialized enzyme, can help maintain telomere length and prevent cellular senescence [5, 6]. Despite its crucial role, telomerase activity decreases with age, and it is frequently undetectable in many human cells. However, it remains detectable in certain cells such as germline cells, cancer cells, and actively dividing peripheral blood mononuclear cells [12, 13, 14].

Cognitive Decline in Aging;

Aging is commonly associated with changes in brain function, particularly cognitive decline. Synchronous neural firing, involved in generating rhythmic oscillatory activity in the brain, can be measured using scalp EEG [16, 17]. This activity is defined by parameters like power, peak frequency, and phase. Changes in these parameters have been linked to neurocognitive functions [18, 19, 20]. Furthermore, alterations in the power and frequency of oscillatory brain waves have been extensively studied in aging, providing insights into how neurocognitive functions change over time [21].

Health Implications of Aging;

With the increase in life expectancy, society faces the challenge of addressing the health issues related to aging. Common causes of death among the elderly include respiratory diseases, heart disease, cancer, and stroke. Chronic conditions such as arthritis, diabetes, osteoporosis, Alzheimer's disease, depression, psychiatric disorders, Parkinson's disease, and age-related urinary problems are prevalent in older adults [22]. Aging also increases the risk of various diseases, with approximately two-thirds of the 150,000 people who die each day worldwide dying from age-related causes [23]. The elderly population, defined as individuals aged 65 and older, is growing rapidly. This shift places additional strain on healthcare systems, pension funds, and the workforce. The elderly dependency rate, which compares the number of elderly to the working-age population, highlights the challenges societies face as their populations age [24]. Regional disparities in elderly populations further exacerbate social and economic challenges [25].

Sensory and Motor Impairments in Aging;

Peripheral neuronal weakening brought on by aging can alter sensation, muscle strength, balance, and gait. Decreased tactile sensitivity, visual impairments, and hearing loss are all caused by declining nerve transmission and compromised sensory feedback. Muscle strength and coordination are weakened by decreased neuromuscular efficiency, which causes postural instability and shorter reaction times. These modifications raise the possibility of falls and problems with mobility. Addressing age-related decreases in motor control and balance is still difficult, even if assistive technology like hearing aids and corrective lenses can help with some sensory deficiencies. Additionally, neurological diseases like Parkinson's disease can hasten the decline of motor and sensory abilities.

The Role of *Bacopa Monnieri* in Cognitive Health;

Bacopa monnieri, an herb used in Ayurvedic medicine, has been traditionally utilized to enhance memory, learning, and cognitive function. It is known for its sedative and anti-epileptic properties [26]. Despite its historical use, there has been limited scientific research on the efficacy of *Bacopa monnieri* decoctions, such as the BMFD, in stabilizing the aging process and related cognitive decline. Although *Bacopa monnieri* is widely recognized for its memory-enhancing effects, there is no scientifically proven evidence on its effects on telomerase activity, telomere length, and neurocognitive functions, particularly in elderly individuals [27]. While telomerase activity and telomere length can be measured in human blood mononuclear cells, cognitive function requires neuropsychological assessment and cannot be directly detected in blood.

Research Gaps and Study Purpose;

This study aims to evaluate the potential of BMFD decoction in stabilizing the aging process and influencing neurocognitive functions in the elderly. There is limited scientific evidence on its effects on telomerase activity, telomere length, and cognitive changes associated with aging, particularly in relation

to *Deha Prakriti* (Body Constitution). By examining these effects, this study seeks to explore how BMFD decoction could support healthy aging and neurocognitive functions. The findings may contribute to developing personalized interventions, including dietary modifications, lifestyle adjustments, and herbal supplementation, to mitigate age-related cognitive decline and enhance overall well-being.

Methods

Study design

This is a two-arm, open-label, non-inferiority randomized controlled clinical trial that will be conducted at the Clinical Trial Center, Faculty of Indigenous Medicine, University of Colombo, Sri Lanka. The test product will be BMFD, a freeze-dried formulation of *Bacopa monnieri*. The trial will evaluate the effects of the *Bacopa monnieri* herbal supplement on aging, neurocognitive functions with relation to Constitution (*Prakriti*), and constitution (*Prakriti*) in healthy adults, compared to a placebo. Participants with (The MoCA score of 24 or above) will be randomly assigned to one of two arms following a 1-week run-in period, with the BMFD herbal supplement administered orally for 45 days. This study protocol has been developed in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines (see Additional file 1). Ethics approval has been obtained from the Ethics Review Committee, Faculty of Indigenous Medicine (ERCFIM), University of Colombo, Sri Lanka (ERC-23/202). The trial is registered in the ISRCTN registry under trial number ISRCTN64126920 <https://doi.org/10.1186/ISRCTN64126920> (see Additional file 2).

Study setting

The study will be conducted at the Clinical Trial Center, Faculty of Indigenous Medicine, University of Colombo, Sri Lanka. Participants will be recruited from healthy individuals, with The MoCA score of 24 or above). Recruitment will take place through a newspaper advertisement inviting individuals to participate in the trial at the Clinical Trial Center, Faculty of Indigenous Medicine, University of Colombo.

Participants

Participation in this research project is voluntary. Participants will be recruited through a screening process to assess eligibility based on inclusion and exclusion criteria. Eligible individuals will then be randomly assigned to either the BMFD decoction group or the placebo group.

Inclusion and exclusion criteria

The inclusion criteria include (1) Healthy individuals aged between 60–64 years at the time of enrollment, of either sex; (2) Nonsmokers and non-alcoholic (3) The MoCA (The Montreal Cognitive Assessment) score of 24 or above. Participants will not be permitted to take any other medications during the trial period. If they need to take any additional medication, they must notify the investigators

and withdraw from the trial. The exclusion criteria include: (1) Individuals with Chronic diseases e.g. Kidney Disease, Cardiovascular Disease, Liver disorders, psychiatric illnesses, Diabetes Mellitus, cancers, Hypertension, hyperlipidemia;(2) Those with reduced capacity to complete the tasks involved in the study.

Sample size;

Sample size calculation for proportions (two-group, two-arm clinical trial) [28] was based on the assumption that, as per the given reference, in most two-arm clinical trials, the predicted outcome from the interventional group (p1) was 30%, and the predicted outcome from the placebo group (p2) was 10%. The outcomes being assessed in this study include cognitive impairment, telomerase activity, telomere length, nerve conduction function, and electroencephalography (EEG). Specifically, the study expects a 30% improvement in the interventional group (BMFD) compared to a 10% improvement in the placebo group for these outcomes. Due to the unavailability of similar research related to the current study, the proportion outcome ratio was taken as 2:1 for groups 1 (interventional group) and 2 (placebo group). The sample size was calculated for a significance level (α) of 5% and a power of 80%. Using these parameters, the calculated sample size was 34 per group. Accounting for an expected dropout rate of 10%, the minimum required sample size per arm was determined to be 37.

Recruitment;

Individuals interested in participating in this clinical study will receive a detailed Patient Information Leaflet (PIL), which will be accompanied by a verbal explanation of the study procedures. If participants agree with the information provided in the PIL, they will then complete a screening questionnaire. Written informed consent will be obtained from each participant by the investigators prior to the initial interview. During the initial interview, participants will undergo a comprehensive history taking, physical examination, and various hematological and biochemical investigations (including FBS, FBC, ESR, ALT/AST, serum creatinine, and UFR). Recruitment based on MoCA analysis score (The MoCA score of 24 or above [29],[30],[31],[32],[33],[34]) Participants who meet the inclusion and exclusion criteria will be recruited for the study. All baseline assessment forms (including the MoCA analysis form, *Prakriti* analysis (constitution), Quality of Life questionnaire) will be completed by the investigators. Participants will not be permitted to take any other medications during the trial period. If they need to take any additional medications, they must inform the investigators and discontinue participation in the trial.

Baseline assessment

The Montreal Cognitive Assessment (MoCA) test, the Nerve Conduction Test (NCT), electroencephalography (EEG), constitutional analysis, and health-related quality of life (HRQoL) will be assessed at baseline. Additionally, hematological and biochemical investigations, including fasting blood sugar (FBS), full blood count (FBC), erythrocyte sedimentation rate (ESR), alanine

aminotransferase/aspartate aminotransferase (ALT/AST), serum creatinine, and urine full report (UFR), will be conducted.

Randomization

The randomization sequence will be generated using an online randomization tool (www.randomisation.com). Block randomization will be applied with blocks of 12 to create a randomization schedule for 74 participants. Patients will be assigned to treatment groups based on the generated sequence. A one-week supply of the assigned investigational product will be distributed to the patients according to their random allocation. The allocation ratio will be 1:1 for each group. Each randomization number's corresponding allocation will be placed into individually sealed, opaque envelopes. These envelopes, along with the allocation sequence, will be securely stored by an investigator who is not involved in patient recruitment. Participants who meet the inclusion and exclusion criteria will be enrolled in the study and assigned a randomization number sequentially, based on the date and time of their recruitment. The treatment indicated in the sealed envelope for each number will then be provided to the corresponding patient. A flowchart depicting the study design is presented in Fig. 1.

Intervention

Intervention *Bacopa moneri* herbal supplement (BMFD) -Arm 1

BMFD was prepared following the traditional method for decoction preparation [35]. Sixty grams of freeze-dried *Bacopa monnieri* (L.) Wettst was boiled with 1920 mL of water over a mild flame until the volume reduced to 240 mL. The decoction was then filtered through a single-folded cotton cloth and collected in a separate vessel. A 60-gram pack of freeze-dried *Bacopa monnieri* (BMFD) will be used to prepare the decoction required for one day. A one-week supply, consisting of seven packs, will be provided to each participant. Patients will be instructed to place the supplied herbal pack into a pot, add 1920 ml of water, and simmer it over low heat until the volume is reduced to 240 ml. The preparation process, carried out under standardized conditions, will be demonstrated to participants assigned to the BMFD arm at the clinical trial center of the Faculty of Indigenous Medicine (FIM) through a video. Participants will be instructed to consume a daily dose of 120 ml, taken twice a day before meals.

BMND; *Bacopa monnieri* (L) Wettst Normal decoction, BMFD; *Bacopa monnieri* (L) Wettst freeze dried decoction, BMPD; *Bacopa monnieri* (L) Wettst Phanta decoction (Hot infusion).BMD; *Bacopa monnieri* (L) Wettst Freeze dry powder, BMFDP; *Bacopa monnieri* (L) Wettst Freeze dry powder.

Placebo – Arm 2

To prepare the placebo while minimizing antioxidant content, freeze-dried green tea leaves will undergo a repeated steeping process. First, the leaves will be placed in 1920 ml of boiling water and simmered for

30–60 minutes, after which the liquid will be discarded. This process will be repeated two to three times with fresh water to further reduce the antioxidant content. Afterward, the treated leaves will be freeze-dried to restore their original form. A 60-gram pack of these processed freeze-dried green tea leaves will be used to prepare the placebo decoction for one day. The preparation process, carried out under standardized conditions, will be demonstrated to participants in the placebo group at the clinical trial center of FIM through a video. Participants will be instructed to consume a daily dose of 120 ml, taken twice a day before meals.

Storage, packaging, and dispensing of investigational herbal supplement and placebo;

Both products (BMFD and placebo) will be packaged for a 7-day supply and labeled with relevant details, including the batch number, dosage, time of administration, and mode of administration. These packages will be securely stored at the clinical trial center of the Faculty of Indigenous Medicine (FIM), University of Colombo, Sri Lanka, and will be dispensed to participants based on the predetermined randomization sequence. A 7-day supply of the investigational products will be provided to study participants during their weekly visits, along with appropriate instructions.

Table 1
Investigational products

Herbal supplement	Dose	Mode of administration	Route	Method of preparation
BMFD	120 ml	Morning and evening before meals	Oral	60 g (BMFD) of Freeze-dried leaves of plant materials boiled with 1920ml of water and reduced to 240ml
Placebo	120 ml	Morning and evening before meals	Oral	Placebo

Storage, packaging, and dispensing of investigational supplement

Outcome measurements;

Primary outcomes;

The following primary outcome measures are assessed at baseline, 45 and 90 days:

1. Cognitive impairment will be measured using the Montreal Cognitive Assessment (MoCA) validated for the Sri Lankan population.
2. Telomerase activity and telomerase length of blood mononuclear cells of participants measured using qualitative polymerase chain reaction (QPCR).
3. Median nerve and Ulnar for upper limb function and Tibial and Common peroneal nerve for lower limb function measured using the nerve conduction test (NCT).
4. Electrical activity of the brain measured using electroencephalography (EEG).

Secondary outcomes;

Health-related quality of life (HRQoL) measured using an HRQoL questionnaire (Janković, Slobodan M., et al. 2021) at baseline and the end of the intervention (after 45 days, 90 days of follow-up).

Safety assessment;

Each participant will undergo hematological and biochemical assessments, including fasting blood sugar (FBS), full blood count (FBC), erythrocyte sedimentation rate (ESR), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and serum creatinine/glomerular filtration rate (GFR), along with a comprehensive urine analysis, both before and after the intervention. These evaluations primarily serve as a safety assessment measure. Adverse events experienced by participants will be systematically recorded on a weekly basis by investigators during scheduled visits to the clinical trial center. Additionally, participants will be instructed to document any adverse reactions in their diaries and promptly report them using the designated contact numbers. In the event of unexpected symptoms or concerns, they will be advised to visit the trial center at the Faculty of Indigenous Medicine for further evaluation. Any serious adverse events will undergo thorough assessment and will be reported to the Ethics Review Committee (ERC) of the Faculty of Indigenous Medicine within five working days. Although no severe adverse reactions are anticipated with BMFD Herbal supplement, in cases where an adverse reaction necessitates hospitalization, appropriate medical care and expert management will be ensured. If at any point the safety of trial participants can no longer be guaranteed or new scientific evidence emerges indicating potential risks, the clinical trial will be prematurely terminated.

HRQoL -Health-Related Quality of Life

Data handling, record keeping, and dissemination;

Each participant will have an individual file to securely store hard copies of case record forms, including informed consent, results from hematological and biochemical investigations, physical examination findings, completed questionnaires, NCT and EEG Data, Moca test data and QPCR analysis data. Data entry will be performed by a limited number of dedicated staff members and saved on a password-protected, dedicated computer. These data will remain with the researchers and will not be shared with any third party under any circumstances. Participant information will be securely stored during each clinic visit throughout the study. Upon study completion, all records will be securely retained for a period of 10 years. Participant data will be stored at the Department of Basic Principles, Ayurveda Anatomy, and Physiology, Faculty of Indigenous Medicine, University of Colombo. These data will be used exclusively for statistical analysis and scientific reporting. Identifying information, such as contact details, will be stored separately from research data. Each participant and their corresponding data will be assigned a unique study identification number. After the study concludes, all databases will be de-identified and archived. A Data Safety Monitoring Board, composed of three independent experts, has been appointed in accordance with the guidelines set by the Ethics Review Committee of the Faculty of Indigenous Medicine to ensure safety monitoring. As this is a single-center trial involving only 74 participants, no

audit is planned for this study. The study results will be disseminated through scientific conferences and peer-reviewed journals. Additionally, individual participants will receive their study results and group allocation information upon the trial's completion.

Ethical considerations;

The research project protocol has received approval from the Research and Higher Degrees Committee of the Faculty of Medicine, University of Colombo, as well as the Ethics Review Committee of the Faculty of Indigenous Medicine (FIM), University of Colombo. The trial has been registered with the ISRCTN registry under the trial number (ISRCTN64126920 -(<https://doi.org/10.1186/ISRCTN64126920>)). The study will be conducted in strict adherence to Good Clinical Practice (GCP) guidelines. Any protocol modifications will be submitted to the Ethics Review Committees and updated in the trial registry for approval. Participants will be provided with an information sheet detailing the research in Sinhala, Tamil, and English, and written informed consent will be obtained prior to participation. The information will include the study's purpose, duration, and potential consequences. Participants will retain the right to withdraw their consent and discontinue participation at any time without any penalty, effect on their medical care, or loss of benefits. The questionnaire will be administered by an interviewer and will remain anonymous. Only essential socio-demographic data, such as occupation and the nature of the participant's health condition, will be collected. No additional personal data will be gathered by the researchers.

Method of data analysis;

For both primary and secondary outcome measures, mean values at baseline and study completion, as well as mean differences, will be compared across the two study arms using ANOVA (Analysis of Variance) or the non-parametric Kruskal–Walli's test, depending on the data's normality. Within each treatment arm, changes in primary and secondary outcomes before and after the intervention will be analyzed using either paired-sample t-tests or the non-parametric Wilcoxon signed-rank test, based on the distribution of the data. For all normally distributed outcomes, 95% confidence intervals will be calculated. Categorical variables will be analyzed between groups using the Chi-square test. Potential confounding factors will be adjusted using ANCOVA, with adjusted mean values and corresponding confidence intervals subsequently calculated and reported. Statistical analysis will be conducted using the SPSS software (version 20.0), and the level of significance will be set at $\alpha = 0.05$. In cases of missing outcome data, the most recent available values of the outcome measures will be used as replacements. Intention-to-treat analysis will be applied for all efficacy and safety outcomes. Additionally, per-protocol analysis will be conducted for efficacy outcomes, including only participants who complete the follow-up.

Discussion

As per modern science, Aging is the time-dependent, physiological decline of biological processes that are often associated with age-related diseases. Those pathologies often associated with aging, such as

cellular inflammation and atherosclerosis, involve hyperactivity or uncontrolled cellular growth. There are about nine hallmarks of aging: genomic instability, telomere attrition, epigenetic alteration, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intracellular communication [36]. The hallmark of anti-aging action is calorie restriction (CR), which involves the extension of the life span and the suppression of age-related diseases. Calorie restriction mechanisms play a major role in modulating chronic inflammation at the molecular level, the impact of epigenetic chromatin and histone modification, and the ultimate control of gene expression [37]. Changes in telomere length and telomerase activity could provide valuable insights into the potential influence of *Bacopa monnieri* on aging-related processes. Since telomere shortening is a hallmark of cellular aging and genomic instability, any modulation in its length may indicate an impact on biological aging. Similarly, alterations in telomerase activity could reflect the extent to which *Bacopa monnieri* influences cellular longevity and regenerative capacity. Investigating these changes will help determine whether *Bacopa monnieri* plays a role in slowing down aging-related cellular decline or enhancing genome stability.

Gene sequences called telomeres are found at the ends of chromosomes and are in charge of preserving the integrity of the genome. Telomere length is at its maximum at birth and decreases progressively with advancing age; thus, it is considered a biomarker of chronological aging. Telomerase is the enzyme responsible for maintaining the length of telomeres by adding guanine-rich repetitive sequences. Telomerase activity is exhibited in gametes, stem cells, and tumor cells. Our research team has designed a two-arm, open-label, non-inferiority randomized controlled trial to evaluate the effects of a freeze-dried *Bacopa monnieri* formulation on aging, neurocognitive functions, and constitution (*Prakriti*) in healthy adults, compared to a placebo and his clinical trial will provide evidence-based scientific data on the effectiveness of *Bacopa* and its Ayurvedic dosage form, BMFD, in the aging process and cognitive enhancement concerning individual constitution (*Prakriti*). This trial is expected to contribute to the early diagnosis of neurocognitive impairment and aging-related neurophysiological changes in relation to individual constitution (*Prakriti*).

Strengths and limitations;

This randomized controlled clinical trial evaluates the effects of a freeze-dried formulation of the *Bacopa monnieri* herbal supplement on aging and cognitive function in relation to constitution (*Prakriti*) in healthy adults and Multiple outcome measures, including neurocognitive function, telomerase activity, telomere length, nerve conduction tests (NCT), and electroencephalography (EEG), provide a comprehensive assessment of the intervention's effects. (Participants The MoCA score of 24 or above will be recruited. The findings of this study will offer valuable evidence supporting the use of this herbal preparation in managing age-related neurocognitive decline and neurodegenerative conditions. The study is conducted within a specific population, which may limit the generalizability of the findings.

Trial status;

This protocol is version 1. The recruitment will be initiated in May 2025 and it is expected that the recruitment will be completed by the end of November 2025.

Declarations

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Authors' contributions;

The study was conceptualized by PKP, HLNRP, WPR, SN, DWDN. The protocol was developed by PKP, HLNRP, DWDN, WPR, and SN. Statistical advice and method of analysis were provided by GL. Clinical trial will be conduct by all the investigators collectively. All authors read and approved the final manuscript

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Availability of data and materials;

Not applicable. This manuscript is a protocol for a randomized clinical trial and does not contain any data.

Ethics approval and consent to participate;

Ethics approval for this clinical trial was granted by Ethics Review Committee of the Faculty of Indigenous Medicine, University of Colombo, Sri Lanka. The trial is registered in the ISRCTN registry under trial number (ISRCTN64126920 -(<https://doi.org/10.1186/ISRCTN64126920>). The study is conducted in compliance with Good Clinical Practice (GCP) guidelines. Written informed consent will be obtained from all participants (refer to Additional file 3). Participants will have ample opportunity to ask questions and carefully consider their decision to participate in the study.

Consent for publication;

Not applicable.

Competing interests;

No competing interests

Author details;

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Table 2

Table 2 is available in the Supplementary Files section.

Additional files

Additional files 1-3 are not available with this version.

Figures

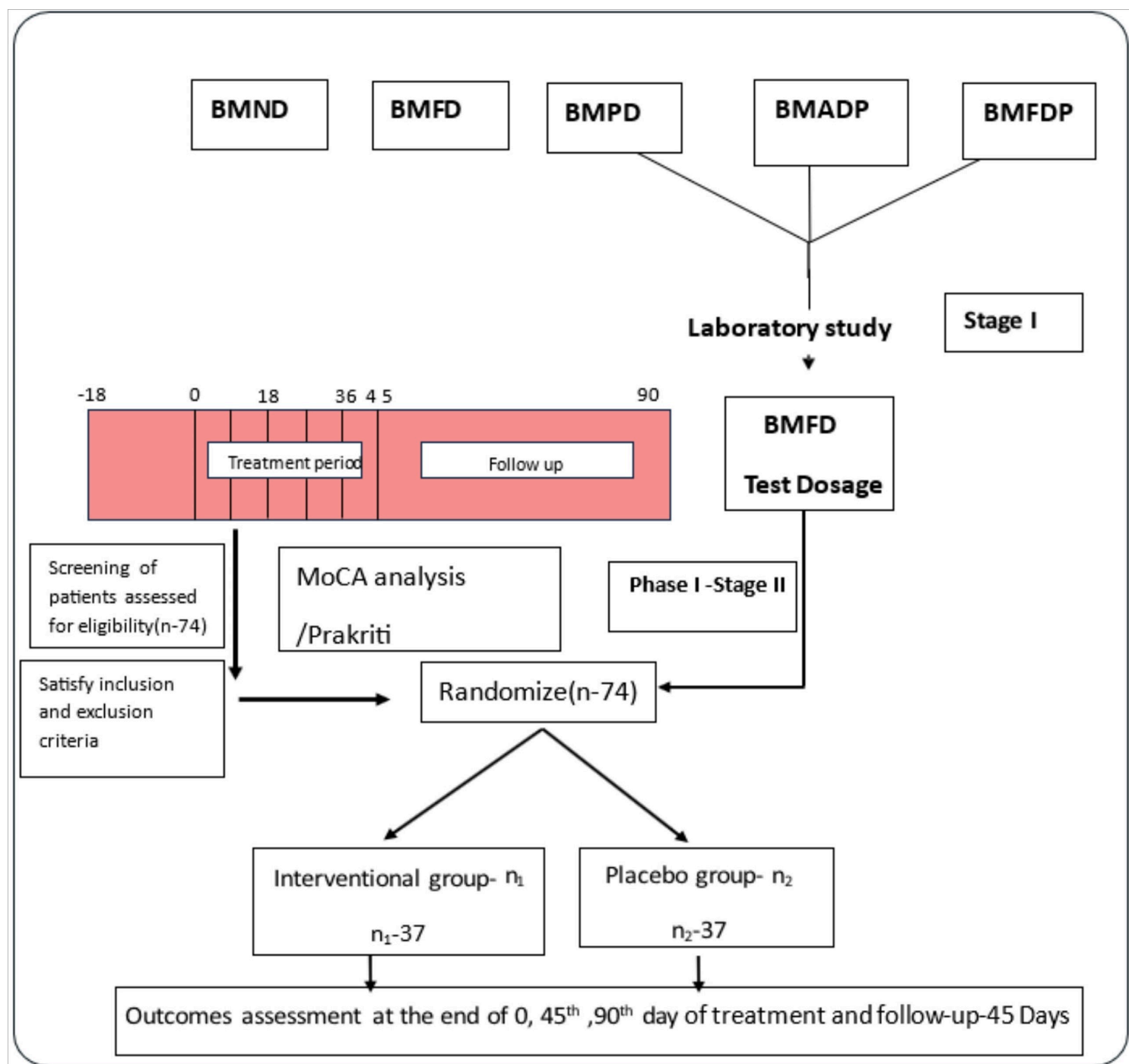


Figure 1

A flowchart depicting the study design.

Supplementary Files

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