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Safety and Efficacy of Khamira Gawzaban Sada (KGS) in Mild Cognitive Impairment: A Pilot Open-Label Clinical Trial

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ABSTRACT

Background: *Mild cognitive impairment (MCI), termed Zu'f al-Dimagh in Unani medicine, is a clinically significant precursor to dementia with limited pharmacological options.*
Objective: *To evaluate the efficacy and safety of Khamira Gawzaban Sada (KGS), a standardized Pharmacopoeial Unani compound, in patients with MCI.*
Methods: *An open-label, single-arm pilot trial enrolled 100 participants (screened n=150) with MMSE scores of 10–23. KGS was administered orally at 10 g/day for six weeks. Primary outcome was change in MMSE score; secondary outcome was patient-reported Quality of Life (QoL). Safety was monitored through adverse event surveillance, laboratory parameters, and vital signs at baseline, Week 2, Week 4, and Week 6.*
Results: *Mean MMSE scores improved significantly from 16.2 (±2.8) at baseline to 22.4 (±1.9) at Week 6 ($p<0.001$). QoL domain scores demonstrated consistent improvement across all measured domains. No serious adverse events were recorded.*
Conclusion: *KGS demonstrates preliminary efficacy and acceptable tolerability in MCI. Randomized controlled trials with larger cohorts are warranted to confirm these findings.*

Keywords*: Khamira Gawzaban Sada; MMSE; mild cognitive impairment; Unani medicine; Zu'f al-Dimagh; Quality of Life; cognitive enhancer.*

1. Introduction

Mild cognitive impairment (MCI) is characterized by objective cognitive decline exceeding that expected for age and education, without sufficient severity to impair activities of daily living. Epidemiological data project a global prevalence of MCI approaching 15–20% in adults over 65 years [1]. Critically, approximately 10–15% of MCI cases convert to Alzheimer's disease annually, underscoring the urgency of early intervention [2]. Despite this clinical burden, no disease-modifying pharmacological agent has been approved for MCI, and currently available cholinesterase inhibitors exhibit limited long-term tolerability. In the Unani system of medicine, cognitive impairment is conceptualized as *Zu'f al-Dimagh* (cerebral weakness) and attributed to diminished cerebral perfusion, dysregulation of *Balgham* (phlegmatic humour), and excessive psychosocial stress [3]. Therapeutic interventions are accordingly directed at cerebral tonification and humoral rebalancing.

Khamira Gawzaban Sada (KGS) is a Unani compound preparation formalized in the National Formulary of Unani Medicine (Part-V, CCRUM, 2008). Its principal bioactive constituents include *Borago officinalis* (borage), which exhibits documented anxiolytic and nootropic effects, and *Melissa parviflora* (lemon balm), with established acetylcholinesterase-inhibitory properties [4]. Despite its longstanding empirical use, rigorous clinical evidence quantifying its cognitive benefit remains absent. The present study was designed to address this evidence gap through a structured pilot clinical evaluation.

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Materials and Methods

2.1 Study Design

An open-label, single-arm, prospective clinical validation study was conducted at the General Outpatient Department (GOPD), Regional Research Institute of Unani Medicine (RRIUM), Mumbai. The study protocol was approved by the Institutional Ethics Committee (Approval No.: RRIUM/IEC/2023) and registered with the Clinical Trials Registry of India (CTRI). Written informed consent was obtained from all participants prior to enrolment.

2.2 Participants

Of 150 screened candidates, 100 fulfilled eligibility criteria and were enrolled.

Inclusion criteria comprised: age 40–75 years; MMSE score 10–23 (indicative of mild–moderate impairment); subjective cognitive complaints corroborated by a reliable informant; and willingness to comply with the study schedule.

Exclusion criteria included: dementia or major neurocognitive disorder; significant psychiatric comorbidity; chronic systemic illness requiring concurrent pharmacotherapy; pregnancy or lactation; and prior exposure to Unani cognitive formulations within 30 days of screening.

2.3 Intervention

Khamira Gawzaban Sada was dispensed as a standardized semisolid oral preparation at a dose of 10 g once daily, administered before breakfast, for a continuous period of six weeks. The preparation conformed to the specifications outlined in the National Formulary of Unani Medicine (CCRUM, 2008). No concomitant cognitive-enhancing agents were permitted during the trial.

2.4 Outcome Measures

Primary outcome: Change in MMSE total score from baseline to Week 6. The MMSE is a validated 30-point cognitive screening instrument assessing orientation, registration, attention, recall, and language [5].

Secondary outcome: Change in patient-reported QoL scores across five domains: mental clarity, mood, daily functioning, sleep quality, and social engagement, each rated on a 0–10 Likert scale.

2.5 Safety Assessment

Safety was evaluated through clinical examination, structured adverse event reporting, and biochemical laboratory investigations (complete blood count, hepatic and renal function tests, fasting blood glucose) at baseline, Week 2, Week 4, and Week 6. Vital signs (blood pressure, pulse rate, respiratory rate) were recorded at each visit.

2.6 Statistical Analysis

Descriptive statistics (mean ± standard deviation) were computed for continuous variables. Within-group changes from baseline to Week 6 were analysed using the paired Student's t-test. A p-value <0.05 was considered statistically significant. All analyses were performed using SPSS v.25.0.

3. Results

3.1 Participant Demographics and Baseline Characteristics

The enrolled cohort (n=100) presented a mean age of 58.4 (±8.2) years, with an approximately balanced sex distribution (males: 54%; females: 46%). The mean baseline MMSE score was 16.2 (±2.8), consistent with mild-to-moderate cognitive impairment. Baseline demographic and clinical characteristics are presented in Table 1.

Table 1: Baseline Demographic and Clinical Characteristics (n=100)

Characteristic	n (%)	Mean ± SD
Age (years)	—	58.4 ± 8.2
Male	54 (54%)	—
Female	46 (46%)	—
Baseline MMSE score	—	16.2 ± 2.8
Married	72 (72%)	—
Duration of symptoms (months)	—	14.6 ± 6.1

3.2 Primary Outcome: MMSE Scores

Mean MMSE scores demonstrated a statistically significant progressive improvement across all assessment time-points (Table 2). The mean score increased from 16.2 (±2.8) at baseline to 22.4 (±1.9) at Week 6 (mean change: +6.2 points; p<0.001). The trajectory of improvement and associated standard deviations are illustrated in Figure 1.

Table 2: MMSE Score Progression Over the Study Period

Time-point	Mean MMSE (± SD)	Change from Baseline	p-value
Baseline	16.2 ± 2.8	Reference	—
Week 2	18.1 ± 2.5	+1.9	<0.01
Week 4	20.3 ± 2.2	+4.1	<0.001
Week 6	22.4 ± 1.9	+6.2	<0.001

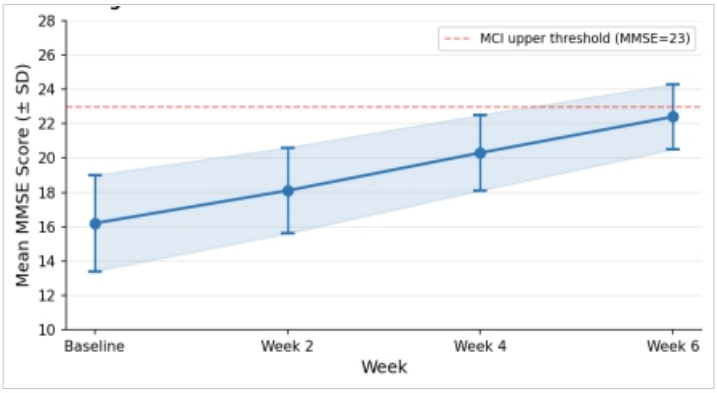

Figure 1: Mean MMSE scores (± SD) at baseline and Weeks 2, 4, and 6. The red dashed line denotes the upper MCI threshold (MMSE=23). Error bars represent ±1 SD.

3.3 Secondary Outcome: Quality of Life

Patient-reported QoL scores improved significantly across all five assessed domains from baseline to Week 6. Mental clarity scores increased from 4.8 to 6.9, mood from 4.2 to 7.1, and daily functioning from 4.5 to 6.8. Sleep quality and social engagement similarly improved. The comparative QoL domain scores are depicted in Figure 2.

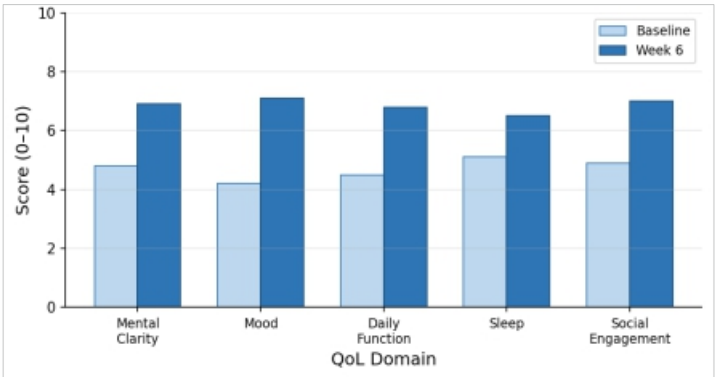

Figure 2. Quality of Life domain scores at baseline and Week 6. Higher scores indicate greater functional well-being (scale 0–10).

3.4 Safety and Tolerability

No serious adverse events (SAEs) were recorded throughout the study duration. Two participants reported transient mild gastrointestinal discomfort (nausea, 2%) in the first week, which resolved spontaneously without dose modification. Haematological and biochemical parameters, including hepatic transaminases, serum creatinine, fasting glucose, and complete blood count, remained within normal reference ranges at all assessment time-points. Vital sign measurements showed no clinically significant deviation from baseline, confirming the tolerability of KGS in this population.

4. Discussion

The present pilot study provides preliminary clinical evidence supporting *Khamira Gawzaban Sada* as an efficacious and well-tolerated intervention for mild cognitive impairment. The observed mean MMSE improvement of 6.2 points over six weeks is clinically meaningful, as a change of ≥3 points is widely considered to represent a minimal clinically important difference in MCI populations [6]. The proposed mechanisms of action of KGS are pharmacologically plausible. *Borago officinalis* contains gamma-linolenic acid, which modulates neuroinflammatory pathways, and triterpenoids with demonstrated cytoprotective properties [4]. *Melissa parviflora* has been shown to inhibit acetylcholinesterase, thereby augmenting central cholinergic transmission in a manner analogous to approved cholinesterase inhibitors [7]. The Unani theoretical framework posits that KGS restores optimal cerebral temperament (*Mizaj*), enhancing mnemic faculty through rebalancing of cerebral humours—a conceptual model that partially overlaps with contemporary neuroinflammatory and neurohumoral hypotheses of cognitive decline. The absence of hepatotoxicity and the benign adverse event profile are particularly notable, given concerns regarding the long-term tolerability of conventional cholinesterase inhibitors. These findings are consistent with prior preclinical safety evaluations of KGS, which demonstrated no organ toxicity at doses exceeding the therapeutic range in rodent models.

Limitations: The single-arm, non-comparative design precludes estimation of placebo response contribution. The six-week follow-up duration is insufficient to assess durability of cognitive benefits or MCI-to-dementia conversion rates. Heterogeneity in MCI aetiology and the absence of neuroimaging or biomarker data constitute additional limitations. Standardization of the MMSE across different educational backgrounds in the study population represents a further methodological consideration.

5. Conclusion

Khamira Gawzaban Sada demonstrates significant improvements in cognitive function as measured by MMSE and patient-reported quality of life over a six-week treatment period, with a favourable safety and tolerability profile. These findings support the hypothesis that KGS merits evaluation in larger, randomized, placebo-controlled trials incorporating longer follow-up, neuroimaging endpoints, and biomarker assessment to establish its role in evidence-based integrative management of mild cognitive impairment.

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