RESEARCH PROTOCOL

TITLE OF RESEARCH PROPOSAL

Observational Study to Evaluate the Effectiveness of Mobithron® Xtra in Patients with Primary Knee Osteoarthritis Over a 3-Month Period

KEY WORDS

Hyaluronic acid, knee osteoarthritis, mobithron, treatment effectiveness

BACKGROUND/ JUSTIFICATION

Osteoarthritis (OA) is one of the most common chronic musculoskeletal conditions worldwide and a leading cause of pain, reduced mobility, and disability, particularly among the aging population [1][2]. In 2019, OA affected approximately 528 million people globally—a 113% increase since 1990—with the knee being the most commonly impacted joint [2][3][4]. In Malaysian primary care, knee OA is frequently encountered, often during early to moderate disease stages, when patients report pain during ambulation, stiffness, or functional decline [1][5].

Conventional management of knee OA typically includes non-steroidal anti-inflammatory drugs (NSAIDs), intra-articular corticosteroids, and surgical interventions in severe cases. However, many of these options present limitations such as gastrointestinal, cardiovascular, or renal risks with long-term use [5][6]. As a result, there is an increasing demand for safe, non-invasive therapies that can offer rapid symptom relief, especially among older adults and those with comorbidities or contraindications to standard pharmacologic treatments.

Recently, there has been growing interest in nutraceuticals for OA management. Mobithron® Xtra is a proprietary oral formulation combining hyaluronic acid, undenatured type II collagen, and Boswellia serrata extract. These ingredients have individually shown potential anti-inflammatory and chondroprotective properties in previous studies [7-10]. Two studies were conducted in Hospital Universiti Sains Malaysia and Sultan Ahmad Shah Medical Centre @ IIUM using Mobithron® on patients with primary osteoarthritis. The studies concluded that Mobithron® is effective in managing the pain and symptoms of osteoarthritis, increase knee muscle strength, reduce the need for analgesic use and is safe to take for 6-months.

This study aims to evaluate the real-world effectiveness of Mobithron® Xtra in improving pain, stiffness, and functionality in patients with primary knee OA over a 3-month observation period, using validated patient-reported outcome measures.

OBJECTIVES & EXPECTED OUTCOMES

Primary Objective:
To assess the effectiveness of Mobithron® Xtra in reducing pain and symptoms of knee OA, as measured by the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) total score & VAS score over a 3-month period.

Secondary Objectives:
To assess treatment satisfaction using Treatment Satisfaction Questionnaire for Medication (TSQM) v1.4.
To evaluate patients' global impression of change (PGIC).
To identify progressive trends in symptom and motion improvement from baseline to Month 3.
To evaluate the safety profile of Mobithron® Xtra

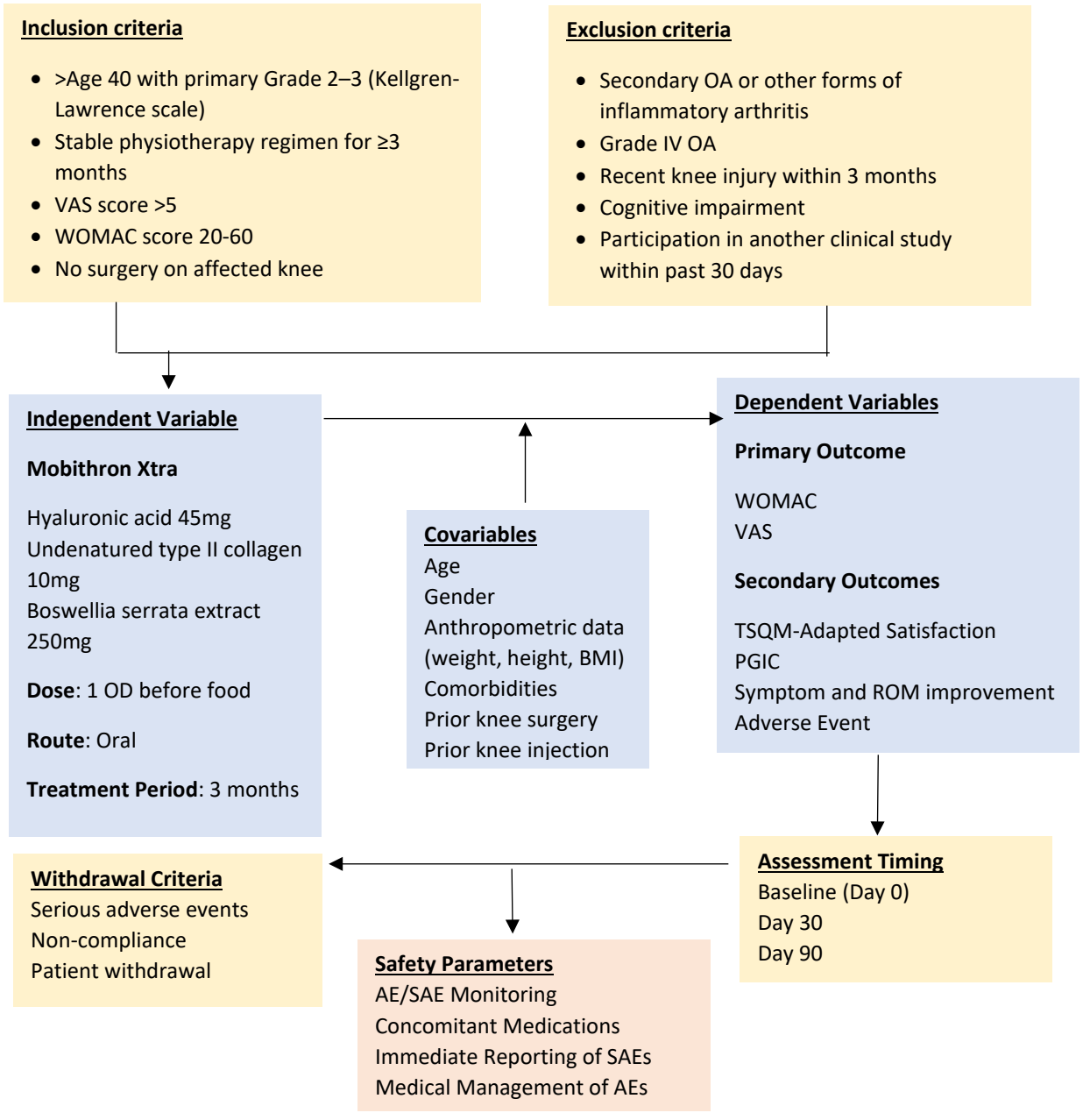
Expected outcomes:
Patients report improvement in pain and symptoms of knee OA evidenced by improved WOMAC and VAS score over 3-month period
Patients report good satisfaction using TSQM v1.4
Patients report good PGIC score
Patients reported progressive improvement in symptoms and motion from baseline to Month 3
Patients reported no adverse effect while on Mobithron® Xtra

METHODOLOGY

Study design

Prospective, multi-centred, observational cohort study, whereby patients fulfilling inclusion and exclusion criteria will be recruited prospectively at 29 general practitioner clinics located throughout Malaysia.

Conceptual Framework (Schematic diagram)



Inclusion criteria
- Adults ≥40 years with primary knee osteoarthritis (OA) (Grade 2–3 on Kellgren-Lawrence scale) till 80 years old
- Clinical and radiographic diagnosis of primary knee OA (Grade II–III on Kellgren-Lawrence scale)
- Stable physiotherapy regimen for ≥3 months
- Baseline VAS score >5
- WOMAC score between 20 and 60
- No prior surgical intervention for the affected knee
- Able and willing to comply with study procedures and provide written informed consent

Exclusion criteria
- Secondary OA or other forms of inflammatory arthritis
- Grade IV OA
- History of recent intra-articular injections within 3 months
- Recent/planned knee surgery
- Severe comorbidities or cognitive impairment
- Participation in another clinical study within the past 30 day

Steps taken to avoid disadvantage of elderly
- Only ambulatory, no cognitive impairment.
- Procedures (WOMAC, VAS, questionnaires) are low burden.
- Extra time allocated for consent explanation and assessments.
- Caregivers allowed to accompany patients.
- Clear withdrawal rights explained.
- Study involves only routine oral supplementation already used in standard practice.

Withdrawal criteria
- Adverse events requiring discontinuation
- Patient request/withdrawal of consent
- Non-compliance with study visits (>1 missed visit)
- Physician decision in patient's best interest

Medications/intervention not permitted during study period
- Intra-articular injections
- New physiotherapy programs

Medications/intervention permitted during study period
- Stable physiotherapy maintained for ≥3 months prior
- Non-OA related chronic medications
- Emergency medications at clinician justification

Participants can continue routine standard care treatment.

Compliance monitoring
Compliance monitored through:
- Daily patient treatment diary (intake ticked daily).
- Capsule count at each visit.

The safety parameters, procedures for eliciting reports of and for recording and reporting adverse event and intercurrent illnesses, and type and duration of follow-up of subjects after adverse events.
- All adverse events (AEs) documented using FP004CRF Adverse Drug Reaction Form

- Safety evaluated at Day 30 & Day 90, and spontaneous reporting at any time.
- Serious AEs reported immediately to investigator.
- Patients with AEs followed until resolution or stable outcome.

Sample size
Test family: F test
Statistical test: ANOVA: Repeated measures, within factors
Effect size (f): 0.25 (moderate)
α (alpha error probability): 0.05
Power (1 – β): 0.95 (high power to detect effect)
Number of measurements (time points): 3 (Baseline, Month 1, Month 3)
Correlation among repeated measures: 0.5
Non-sphericity correction ε: 1 (conservative)

For detecting a moderate effect size (f = 0.25) in a within-subjects repeated measures ANOVA with 3 time points:

Required sample size ≈ 150 participants

Data Analysis
Data analysis will include descriptive statistics to summarise patient characteristics. Repeated measures ANOVA to detect clinically significant improvement in WOMAC, VAS, TSQM and PGIC score

Product information, dosing regimen and assessments
Product: Mobithron Xtra (Hyaluronic acid 45mg, Undenatured Type II Collagen 10mg, Boswellia Serrata Extract 250mg).
Dose: 1 capsule once daily before food
Route: Oral.
Treatment period: 3 months.
Assessment timing: Baseline (Day 0), Day 30, and Day 90.
Parameters:

1. Visual analogue scale (VAS)
2. Western Ontario and McMaster Universities Arthritis Index (WOMAC)
3. Treatment Satisfaction Questionnaire for Medication (TSQM)-adapted Satisfaction
4. Patient's Global Impression of Change (PGIC)
5. Adverse events.

Product Holder:
BREGO LIFE SCIENCES SDN BHD
NO. 5,
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56100
CHERAS

National Pharmaceutical Regulatory Agency (NPRA) status: Mobithron® Xtra is registered and notified under NPRA as a health supplement
Registration number: MAL25046067NC

This study evaluates the product as used in routine clinical practice, consistent with its status as an approved and marketed supplement.

RESEARCH DATA

Where will the data be kept? (Please provide details)
Questionnaire data sheets will be collected individually at each participating clinics during patient recruitment and follow-up. The questionnaire data sheets will be sent to the principal investigator who will then compile the data and key-in to Excel spreadsheet and SPSS statistical software for statistical analyses.

Who will have access to the research data?
Principal investigator

How long will the data be kept? (suggestion: at least 7 years)
7 years

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POTENTIAL IMPACT

We anticipate significant improvement in patients' WOMAC and VAS scores from baseline, with progressive benefits from Month 1 to Month 3. This will support Mobithron® Xtra's role as a symptomatic treatment for moderate primary knee OA (Kellgren-Lawrence Grade II and III).