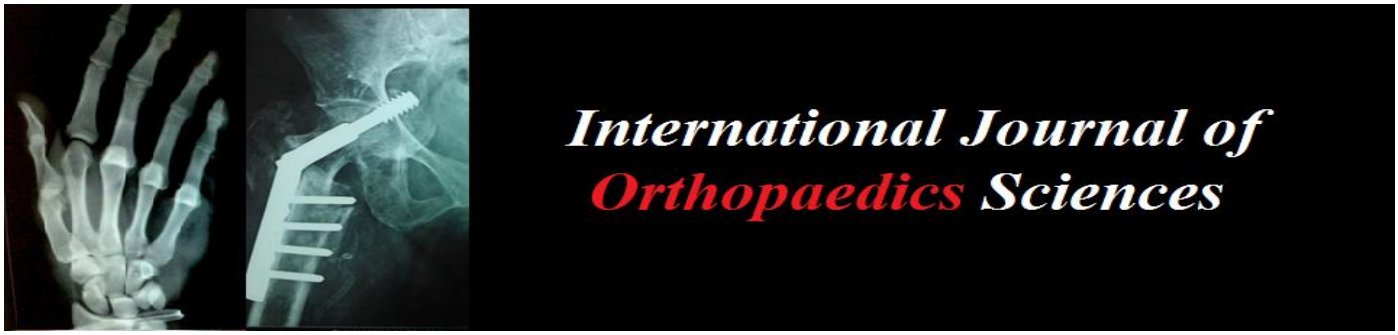

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Effect of Habbe Gule Aakh in osteoarthritis knee: A randomised clinical trail

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Abstract
Background: Osteoarthritis of knee is a chronic degenerative disorder of multifactorial etiology characterized by the loss of articular cartilage, hypertrophy of bone at the subchondral sclerosis. Osteoarthritis knee is managed effectively in Unani system of medicine with Habbe Gule Aakh
Objective: To evaluate the study of different doses of Habbe Gul Aakh in osteoarthritis knee joint
Methods: A randomized single blind parallel arm comparative (dose escalation) study. Habbe Gule Aakh was administered in different doses on 60 patients of osteoarthritis knee in National Institute of Unani Medicine, Bengaluru. Four groups with 15 patients in each, were divided based on Radiological Kellgren Lawrence scale. The subjects of Group I were administered orally with 500 mg, Group II with 1000 mg, Group III with 1500 mg and Group IV with 2000 mg Habbe Gule Aakh, per day in 2 divided doses. The effect of study was assessed with objective parameters of WOMAC (Modified) CRD Pune Questionnaire, Visual Analogue Scale (VAS) was analyzed on 0^{th}, 7^{th}, 14^{th} and 21^{st} day. The data was analysed by ANOVA test, paired t-test, Student t test, and Chi-square/Fisher Exact test for intragroup and intergroup comparisons
Results: The observation of the study reveals that H.G.A orally in group I, II, III and IV for a period 21 days dose escalated as per Grades shows significant improvement(p<0.001) in patients of all groups with objective parameters of WOMAC (modified) Pune Questionnaire and VAS without any adverse effects
Trial registration: Committee (IEC No: NIUM/IEC/2019-20/007/Moal/07 DT 24.09.2020 and registered in CTRI: CTRI/2021/03/031747.

Keywords: Osteoarthritis, OA knee, Kellgren Scale Grade, Habbe Gule Aakh, VAS. WOMAC, Unani Medicine, different dose in different KG Scale Grades

Introduction
Waja-ul-Mafasil (Osteoarthritis) is a broad term which is applied for all types of joints pain [1]. It is the most common degenerative disorder commonly represent pain in major joints especially Knee. It is the most common form of arthritis affecting 1 in 3 people over age 65 and women more than men [2], and it is the 2nd most common rheumatologic problem with most frequent joint disease with a prevalence of 22% to 39% in India. It affects about 4-6% of adult population and is mentioned as one of the top 5 chronic diseases in India [3]. Globally, among the Non communicable diseases Osteoarthritis was one among the top musculoskeletal disorders [4].
In *Unani system of medicine* osteoarthritis can be correlated with "Wajaul Mafasil". The word 'Waja-ul-Mafasil' is made of "Waja" literally means pain, "Mafasil" the 'joints'. Some physicians considered that "Tahajjar-ul-Mafasil (lock joint)" meaning stone like joint as an equivalent term for OA as there is restricted movement of joint. But it is because of degeneration and the term "Waja-ul-Mafasil" is a better term as the main complaint of the patient is pain in knee joint. According to Unani system of medicine which is based on the fundamentals of Humoral Theory [5]. A cause of pain is described as humoral imbalance. When morbid matter gets accumulated in joints as there is empty space, that becomes thick and hard, based on the type of morbid matter [6]. According to Unani system of medicine the predisposing factors of Osteoarthritis, Sue Mizaj Saada(without matter) or Sue Mizaj Maddi (with matter) due to accumulation of Ghairtabayi Akhlat (abnormal humor), which could be due to Damavi (sanguine), or Safravi (choleric), or Balghami(phlegmatic), or saudavi(melancholic) Khilt (humour), or a mixture of any two Ghairtabayi Akhlat [6].

As the 'Mizaj' (temperament) of the patients is usually cold and Wet the morbid matter may be either Sauda or Balgham. There are multiple other factors such as age, chronic diseases, post menopause, trauma and heredity, etc [7].

Osteoarthritis is empirically treated with NSAIDs, Aspirin, Colchicines, Cox-2 inhibitors, intra-articular steroids etc [8] and Surgical intervention in conventional medicine, but the major disadvantages reported with these are many adverse and serious side effects that include Gastrointestinal (Dyspepsia, Gastritis, Peptic Ulcer and Gastro Intestinal bleeding, etc.), Renal (Renal papillary necrosis, Acute Interstitial nephritis, hyperkalemia and sodium retention) and Cardio Vascular(Hypertension, Myocardial Infarction, Cardiogenic stroke, Atrial Fibrillation) implications[10]. In modern medicine the management of Osteoarthritis is NSAIDs,

In Unani Medicine, Osteoarthritis is managed with regimens and drugs which comprises a number of single drugs such as Asgand (Withania somnifera Dunal.), Baboona (*Matricaria chamomilla* Linn.), Suranjan (Colchicum Luteum Baker), Bozidan (*Chrysanthemum indicum* Linn.), Hulba (*Trigonella Foenum-Graecum* Linn), Nakhoona (Trigonella uncata Boiss), etc. and compound drugs such as Habbe Gule Aakh, Habbe Surnjan, Habbe Hudaar, Banadiq Khamsa, Kusthe Godanti, Majoone Azaraqi, Majoone Jograj Gogul, Majoone Chobchini, Majoone Surnjan, Majoone lana, etc., and externally Roghane Kuchla, Roghane Hafth Barg, Roghane Mom, Roghane Surkh, Roghane Chahar Barg, Arq Mom, Khairooti Muhallil, etc [9, 10].

According to modern science osteoarthritis is classified as follows

Primary Osteoarthritis: It is also known as idiopathic osteoarthritis. It is the most common form of the disease. In this type of osteoarthritis, no predisposing factor is apparent [11].

Secondary Osteoarthritis: Several disorders are recognized as causes of secondary Osteoarthritis. They can be divided into Anatomic, Traumatic, and Metabolic Inflammatory causes [11]. A patchy chronic synovitis and thickening of the joint capsule may further restrict movement. Particular muscle wasting is common and leads to instability [11].

Clinical Features

- Pain is the most common symptom.
- Stiffness after inactivity (early morning stiffness, usually < 30 minutes).
- Restriction of movement.
- Muscular weakness.
- Functional limitations and handicap.
- Tenderness around the joint.
- Firm swelling of the joint margin.
- Coarse crepitus (crackling or locking).
- Sign of mild inflammation may be present.
- Tightness of the joint.

Unani system of medicine has a huge resource of herbal, mineral and animal origin drugs, simple and compound drugs to manage Osteoarthritis; and many studies have been conducted in National Institute of Unani Medicine and other Unani research Institutions [8, 12, 13, 14].

The process has been giving Munzij according to the morbid matter (Often Balgham or Sauda), but the main intention is to reduce the pain, so many types of musakkin alam (Analgesics) have been used of which Habbe Gule Aakh [9, 10, 12, 14] is one of the often used drug in condition of pain associated musculoskeletal disorder and very effective in management of Wajaul Mufasil (osteoarthritis), therefore it is intended to evaluate the effect of different doses of Habbe Gule Aakh on radiologically graded Osteoarthritis of knee joint based on Kellgren Lawrence Scale. Hence a study is planned to provide better relief for the Osteoarthritis patients. It is intended to further validate the different doses of "Habbe Gule Aakh" in Wajaul Mafasil.

Materials and Methods

Subjects were selected, who fulfilled the inclusion criteria after obtaining written informed consent were enrolled in the study. Patients were divided into 4 groups based on the grades of Kellgren Lawrence scale in Osteoarthritis of Knee joint. The research was conducted in compliance with Declaration of Helsinki and the principles of Good Clinical practices. This study was conducted over a period of 12 months from 21st, March 2021 to 20th, March 2022 after the approval by the Institutional Ethical Committee (Committee (IEC No: NIUM/IEC/2019-20/007/Moal/07 dt. 24.09.2020 and the Trial was registered in Clinical Trial Registry-India (CTRI/2021/03/031747).

A total of 156 patients were screened for the study, during screening 18 patients in Group-I, 18 patients in Group-II, 24 patients in Group-III, 36 patients in Group-IV did not fulfil inclusion criteria and were excluded from the study.

The research protocol of the study was 21 days divided into 3 follow up (7th, 14th and 21st day. At every follow up, patients were assessed by using objective parameters of WOMAC (Modified) CRD Pune Questionnaire and VAS. All the patients were kept under strict observation for any kind of adverse effect or any kind of parameter worsening.

Criteria for selection of subjects

The patients were enrolled in the study after fulfilling following criteria

Inclusion criteria

1. Diagnosed case of OA Knee Joint as per ACR Criteria (Diagnostic, Laboratorial, and Radiological).
2. Patient of either gender.
3. Patients in age groups of 30-60 years.
4. Grade I, II, III and IV of Kellgren Lawrence grading scale.

Exclusion criteria

1. Patients below 30 years and above 60 years of age.
2. Systemic and metabolic illness like IHD, TB and Malignancy.
3. Patients with other than osteoarthritis.
4. H/o Knee injury, surgery, steroid injection in knee joints.
5. Pregnancy and lactation.
6. Patients under treatment of steroids.
7. Morbid Obesity BMI > 40.

Evaluation of study subjects

History

A detailed history was recorded regarding their chief complaints with duration, age, sex, religion, marital status, occupation, address, socioeconomic status was arrived using Modified Kuppuswamy's Socioeconomic Status Scale 2017, Personal history, treatment history, past history of any disease, family history was also recorded in a predesigned proforma.

Examination
Each patient was subjected to comprehensive general physical and systemic examination. Verbal consent was taken from all the patients prior to examination. General physical and systemic examinations were carried out and vitals were recorded. Specific dermatological examination was also carried out. The information and findings were recorded in the CRF. Assessment of *mizaj* (temperament) was done according to temperament chart attached with the CRF. Eligible patients were subjected to investigations subsequently.

Investigations
Certain investigations were carried out with the aim to exclude the patients with pathological conditions mentioned under exclusion criteria and to assess the efficacy of treatment groups and safety studies were skipped as Habbe Gule Aakh didn't have any toxicological reports till date. Following investigations were carried to assess the patient.

The Following tests were done at baseline.
a. Hb%, TLC, DLC.
b. ESR.
c. Serum glutamic oxaloacetic transaminase (SGOT).
d. Serum glutamic pyruvic transaminase (SGPT).
e. Alkaline phosphatase.
f. Blood urea.
g. Serum creatinine.
h. Complete urine analysis.

Assessment of mizaj: Determination of *mizaj* was done on the basis of *Ajnas-e-Ashra* (10 different parameters) mentioned in Unani literature.

Method of Collection of Data: Data has been collected in case report form
- Method of collection of data.
- By history and subjective symptoms.
- By clinical examination.
- By objective parameters.

Study design
A Randomized single blind parallel arm comparative (dose escalation) Clinical Trial.

Sample size
The sample size was 60 subjects (Group I, Group II, Group III, Group IV) each 15 patient based on previous studies.

Subject Allocation
After screening eligible patients were allocated into concern groups based on the Radiological grades. (Grade I as Group I, Grade II as Group II, Grade III as Group III, and Grade IV as Group-IV) based on Kellgren Lawrence scale.

Duration of protocol Therapy
The treatment period was determined as 21 days (3 weeks).

Criteria for selection of drugs
Habbe Gule Aakh (a compound Unani formulation) which has been used since antiquity and has been prescribed for the management of OA was found very effective [9, 10, 12, 14]. This study was done with hypothesis that to assess the effect of escalated dose as per grading of Kellgren Lawrence Scale, will provide better relief for the OA patients. The raw drugs Barge Bans, Gule Aakh, Zanjbeel and Filfil Siyah were procured from IMPCOPS (Indian Medical Practitioners Co-operative Pharmacy and Stores), Chennai. These ingredients were identified by the chief pharmacist the Department of pharmacy, NIUM. Bangalore and also the drug has been authenticated by the Institute of Trans-Disciplinary Health Sciences and Technology, Bengaluru, where a voucher specimen was retained under code FRLHT Acc. No.5629, 5630,5631 and 5632.
Habbe Gule Aakh was prepared in Pharmacy of National Institute of Unani medicine as per standard GMP protocol. The weight of each pill was 250 mg.

Test drug: Habbe Gule Aakh
Its ingredients are Gule Aakh (*Calotropis procera* Aiton) dried flower, Barge Bans (*Bambusa arundinacea* Willd.) leaves, Zanjabeel (*Zingiber officinalis* Roscoe.) rhizomes, and Filfil Siyah (*Piper nigrum Linn.*) dried fruits all equal quantity by weight.

Patient were treated with dose escalation based of the Kellgren Lawrence Grades
Grade I-250 mg i.e. 1 pill B.I.D = 500 mg/day.
Grade II-500 mg i.e., 2 pills B.I.D = 1000 mg/day.
Grade III-1500 mg i.e., 3 pills B.I.D = 1500 mg/day.
Grade IV-2000 mg i.e., 4 pills B.I.D = 2000 mg/day.

Administration: In pill form for oral administration in two divided doses, was given after food for the period of 3 weeks.

Follow-up and assessment
After fulfilling the inclusion criteria, Habbe Gule Aakh was given to patients with dose according to the Groups which were divided as per the Kellgren Lawrence Grades. The patients were instructed to report immediately if there is any adverse action. Patients were asked to attend the OPD for follow-up weekly i.e., Day of enrolment, 7th day, 14th day and 21st day. The following objective parameters were used for assessment and analysis.

Objective parameters
1. VAS Visual Analogue Scale [15].
2. WOMAC (modified) CRD Pune [16, 17, 18].

The visual analogue scale (VAS) is used in research. The VAS consists of a 10 cm long horizontal line with its extremes marked as 'no pain' and 'worst pain imaginable' (Fig. 6). Each patient ticks their pain level on the line and the distance from 'no pain' on the extreme left to the tick mark is measured in millimetres yielding a pain score from 0 to 10. This self-report of pain is considered as the 'gold standard' of pain measurement [15].
The Western Ontario and the McMaster Universities Osteoarthritis Index is used, they have standardized questionnaires to evaluate the condition of subjects with osteoarthritis of the knee, which includes pain, stiffness, and functional activities of the joints. In this WOMAC scale, measurements are made on pain using five items for pain (score in a range of 0-20), stiffness using two items (score range 0-8), and functional limitation using 17 items (score range between 0-68). The Physical function part contains questions about everyday activities like stair climbing, standing up from a sitting (sit to stand) or lying position, standing, bending from a standing posture, gait, car usage, shopping, putting on and taking off socks, bed mobility, getting in or out of a bath, sitting, and other household

activities [18].

11. Treatment Outcome: The treatment outcome was assessed by analysing through VAS and WOMAC scale on date of enrolment, 7th Day, 14th day and 21st day of treatment.

Outcome: Over all comparison
Comparison intra group and intergroup

Withdrawal criteria

- Failure to follow up.
- Poor compliance to the protocol/disease progression.
- Any adverse effect/disease progression

Adverse drug reaction documentation: No adverse effect of the drug was reported

Documentation

The records were submitted to the Department of Moalajat after completion of the study.

Statistical analysis [19-22]

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance.

The one-way analysis of variance (ANOVA), paired t-test, Student t test, Chi-Square/Fisher Exact test were used for statistical analysis.

Statistical software [23]

The Statistical software namely SPSS 22.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Results

1. **Primary outcome:** Efficacy of HGA by WOMAC (Modified) CRD Pune assessment (Table-1): The study participants of Group I had mean of total WOMAC score 63.13±1.77 on baseline, 58.60±2.56 on 7th day, 55.73±3.06 on 14th day and 51.80±4.28 on 21st day with 500 mg/day HGA. The p value from baseline to all consequent follow up was < 0.001.

   Group II had mean of total WOMAC score 74.27±4.03 on baseline, 61.27±4.18 on 14th day and 55.53±4.81 on 21st day with 1000 mg/day HGA. The p value from baseline to all consequent follow up was < 0.001.

   Group III had mean of total WOMAC score 105.87±2.47 on baseline, 96.00±3.09 on 7th day, 86.80±3.19 on 14th day and 78.27±2.63 on 21st day with 1500 mg/day of HGA. The p value from baseline to all consequent follow up was < 0.001.

   Group IV had mean of total WOMAC score 125.40±2.77 on baseline, 115.07±3.59 on 7th day, 105.47±4.47 on 14th day and 98.40±5.91 on 21st day with 2000 mg/day of HGA The p value from baseline to all consequent follow up was < 0.001.

   The study showed good response with the escalated dose reduces the severity of pain. The efficacy of Habbe Gule Aakh is good in management of pain in osteoarthritis of knee joint with higher dose.
2. **VAS Assessment (Table 2):** Group I patients had mean of pain 7.27±1.10 on baseline, 5.80±1.08 on 7th day, 4.47±0.99 on 14th day and 2.80±0.56 on 21st day with 500 mg/day of HGA. The p value from baseline to all consequent follow up was < 0.001. Group II had mean of pain 7.53±0.92 on baseline, 6.20±0.77 on 7th day, 4.93±0.80 on 14th day and 3.53±0.74 on 21st day with 1000 mg/day of HGA. The p value from baseline to all consequent follow up was < 0.001. Group III had mean of pain 8.93±0.26 on baseline, 6.80±0.68 on 7th day, 5.27±0.80 on 14th day and 3.73±0.70 on 21st day with 1500 mg/day of HGA. The p value from baseline to all consequent follow up was < 0.001. Group IV had mean of pain 8.87±0.35 on baseline, 6.87±0.35 on 7th day, 5.00±0.38 on 14th day and 3.33±0.49 on 21st day with 2000 mg/day of HGA. The p value from baseline to all consequent follow up was < 0.001.
3. **Secondary outcome:** The characteristics (Demographic data) and results are summarized as follows:
4. **Age:** Out of 60 study participants 26(43.3%) were of 51-60 years, 15(25%) of 41-50 years, 11(18.3%) of 30-40 years and 8(13.3%) above 60 years were found.
5. **Gender:** Out of 60 study participants 43(71.7%) female and 17(28.3%) male patients were there.
6. **Occupation:** Out of 60 study participants 36(63.3%) of housewives, 13(21.7%) employed, 6(10%) business persons, 2(3.3%) retired employees and 1(1.7%) Labourers were present.
7. **Marital Status:** All 60(100%) patients were married.
8. Religion: Out of 60 study participants 39(65%) Muslims, 20(33.3%) Hindus and 1(1.7%) Christians were present.
9. **Past history:** Out of 60 study participants 43 (71.7%) didn't have any comorbidity, whereas 31 (21.7%) had DM and 4 (6.7%) had HT.
10. **Duration of illness:** Out of 60 study participants, 35(58.3%) suffered with osteoarthritis of <3 years), 11(18.3%) had duration of 9-12 years, 9(15%) had duration of 3-6 years and 5(8.3%) had duration of 6-9 years.
11. **Dietary Habits:** Out of 60 study participants 55 (91.7) % are of mixed diet and 5(8.3%) were vegetarian.
12. **Life style:** Out of 60 study participants 46 (76.7%) patients had Moderate, 4(6.7%) had Sedentary and 10 (16.7%) Strenuous life style.
13. **Socio economic status:** Out of 60 study participants 31(51.7%) belongs to lower middle (SES III), 26(43.3%) upper middle (SES II), 2(3.3%) upper lower (SES IV) patients and 1(1.7%) upper (SES I) were present.
14. **Addiction:** Out of 60 subjects 55(91.7%) were neither addicted to smoking nor alcohol, 5(6.7%) addicted to smoking and 1(1.7%) addicted to alcohol.
15. **Family history of Osteoarthritis:** All the 60(100%) patients didn't have family history of osteoarthritis knee.
16. **Mizaj:** All the 60(100%) patients were of Balghami mizaj.

Discussion

Primary outcome: The effect of intervention of Habbe Gule Aakh with modified dose on objective parameters was determined over a period of 3 weeks i.e., 21 days using WOMAC (modified) CRD Pune Questionnaire and VAS (Visual Analogue Scale).

WOMAC (modified) CRD Pune Questionnaire assessment Table-1, Graph-1

The study participants of Group I had mean of Total WOMAC 63.13±1.77 on baseline got reduced to 58.60±2.56 on 7th day of treatment, further on 14th day 55.73±3.06 and on 21st day 51.80±4.28 with 500 mg of Habbe Gule Aakh per

day in two divided doses. There is gradual reduction in scale when compared with baseline, 7th day, 14th day and 21st day. The p value from baseline to 7th day was < 0.001, baseline to 14th day was < 0.001 and from baseline to 21st day was < 0.001.

The study participants of Group II had mean of Total WOMAC 74.27±4.03 on baseline got reduced to 67.53±4.63 on 7th day of treatment, further on 14th day 61.27±4.18 and on 21st day 55.53±4.81 with 1000 mg of Habbe Gule Aakh per day in two divided doses. There is gradual reduction in total WOMAC scale when compared with baseline, 7th day, 14th day and 21st day. The p value from baseline to 7th day was <0.001, baseline to 14th day was < 0.001 and from baseline to 21st day was < 0.001. Group III had mean of Total WOMAC 105.87±2.47 on baseline got reduced to 96.00±3.09 on 7th day, further on 14th day to 86.80±3.19 and on 21st day to 78.27±2.63 with 1500 mg of Habbe Gule Aakh per day in two divided doses. There is gradual reduction in total WOMAC scale when compared with baseline, 7th day, 14th day and 21st day. The p value from baseline to 7th day was < 0.001, baseline to 14th day was < 0.001 and from baseline to 21st day was < 0.001. Group IV had mean of Total WOMAC 25.40±2.77 on baseline got reduced to 115.07±3.59 on 7th day, further on 14th day to 105.47±4.47 and on 21st day to 98.40±5.91 with 2000 mg of Habbe Gule Aakh per day in two divided doses. There is gradual reduction in total WOMAC scale when compared with baseline, 7th day, 14th day and 21st day. The p value from baseline to 7th day was < 0.001, baseline to 14th day was < 0.001 and from baseline to 21st day was <0.001. When compared with other groups, the pain on date of enrolment is increased as the Group increases (the patients in Group III and Group IV had more pain in comparison with Group II). The response to the escalated dose reduces pain more.

The more the dose the reduction of pain increased drastically and continuously. The study conducted by Nagashima *et al* also suggest that escalated dose of analgesic better efficacy [24]. The efficacy of Habbe Gule Aakh is good in management of pain in osteoarthritis of knee joint with higher dose.

VAS Assessment (Table 2, Graph 2)

VAS assessment of pain in osteoarthritis of knee joint was done on all four groups and comparison with the baseline findings on 7th day, 14th day and 21st day is compiled. Group I patients had mean of pain 7.27±1.10 on baseline got reduced to 5.80±1.08 on 7th day of treatment, further on 14th day to 4.47±0.99 and on 21st day to 2.80±0.56 with 500 mg of Habbe Gule Aakh per day in two divided doses. There is gradual reduction in scale when compared with baseline, 7th day, 14th day and 21st day. The p value from baseline to 7th day was <0.001, baseline to 14th day was <0.001 and from baseline to 21st day was <0.001. Group II patients had mean of pain 7.53±0.92 on baseline reduced to 6.20±0.77 on 7th day, further on 14th day 4.93±0.80 and on 21st day 3.53±0.74 with 1000 mg of Habbe Gule Aakh per day in two divided doses. There is gradual reduction of pain as per scale when compared with baseline, 7th day, 14th day and 21st day. The p value from baseline to 7th day was <0.001, baseline to 14th day was <0.001 and from baseline to 21st day was <0.001. Group III patients had mean of pain 8.93±0.26 on baseline got reduced to 6.80±0.68 on 7th day further on 14th day 5.27±0.80 and on 21st day 3.73±0.70 with 1500 mg of Habbe Gule Aakh per day in two divided doses. There is gradual reduction of pain in scale when compared with baseline, 7th day, 14th day and 21st day. The p value from baseline to 7th day was <0.001, baseline to 14th day was <0.001 and from baseline to 21st day was <0.001. Group IV Patients had mean of pain 8.87±0.35 on baseline got reduced to 6.87±0.35 on 7th day, further on 14th day 5.00±0.38 and on 21st day 3.33±0.49 with 2000 mg of Habbe Gule Aakh per day in two divided doses. There is gradual and constant reduction in pain scale when compared with baseline, 7th day, 14th day and 21st day. The p value from baseline to 7th day was <0.001, baseline to 14th day was <0.001 and from baseline to 21st day was <0.001. When compared with other groups, the Pain increased as the Group increases (the patients in Group III and Group IV had more VAS severity scale readings in comparison with Group I and II). The response to the escalated dose of Habbe Gule Aakh reduces Pain gradually and constantly. The efficacy of Habbe Gule Aakh with escalated dose shows remarkable results in management of Osteoarthritis of Knee joint.

Secondary outcome

Discussion on the data showing the efficacy of Habbe Gule Aakh based on objective parameters based on demographic data is being presented here to draw inferences. (Age, Gender, Marital status, Religion, Occupation, Socioeconomic status, Mizaj, Dietary habits, Lifestyle, Treatment history, Addiction, Duration of illness, Family history).

1. **Age:** The mean age of the study participants was 51.67±9.89 years, these observations suggest that the age of patients has significance with grades of osteoarthritis knee, as the age increases group also likely to increase (The KL classification) suggesting wear and tear increases. With increase of age the mechanism leading to joint damage is poorly understood but it is a multi-factorial such as oxidative damage, thinning of cartilage, muscle weakening and a reduction in proprioception that occurs with advanced age, which has profound effects on cellular processes notably leading to enhanced apoptosis and reduced cellular regeneration [25]. The descriptions made by Yashpal Munjal [25] and KasperDL [26] that osteoarthritis prevalence rises strikingly with age. The Incidence of osteoarthritis as per literature also suggest that osteoarthritis is common in age group above 50 years[30, 130]. Osteoarthritis is prevalent in 4th and 5th decade of life as per observations of Nayab M[17], Manoj Kumar *et al*[131], Longo D *et al*[123] and Razana MCN[18].
2. **Gender:** According to the gender, out of 60 participants in the study 43(71.7%) were female patients and 17(28.3%) were male patients, in the ratio of 3:1.
3. **Occupation:** According to the occupation of the study participants, out of 60 subjects that 38(63.3%) were housewives, 13(21.7%) employed, 6(10%) business persons 2(3.3%) retired employees and 1(1.7%) labourer. As already seen in gender distribution, females suffer from osteoarthritis more than males. When we consider the occupation, elderly homemakers seem to have more degenerative disorders due to their age factor too. Studies conducted by Razana MCN [14], corelate with this.
4. **Marital Status:** All study participants 60(100%) were married and there is no reliable data showing that the person being single or married is under risk of getting osteoarthritis. The studies of Razana MCN [14] suggest that osteoarthritis knee is prevalent among married. Osteoarthritis is associated with active marital life according to Ibn Sina [7] and Jurjani [6].
5. **Religion:** Out of 60 study participants of this study are 39(65%) were Muslims, 20(33.3%) Hindus and 1(1.7%) Christian. There is no significant correlation of religion

with osteoarthritis. But studies conducted by Razana MCN [14] suggest osteoarthritis is prevalent among Muslims; this might be because the patients visiting the study site are more from Muslim Community.

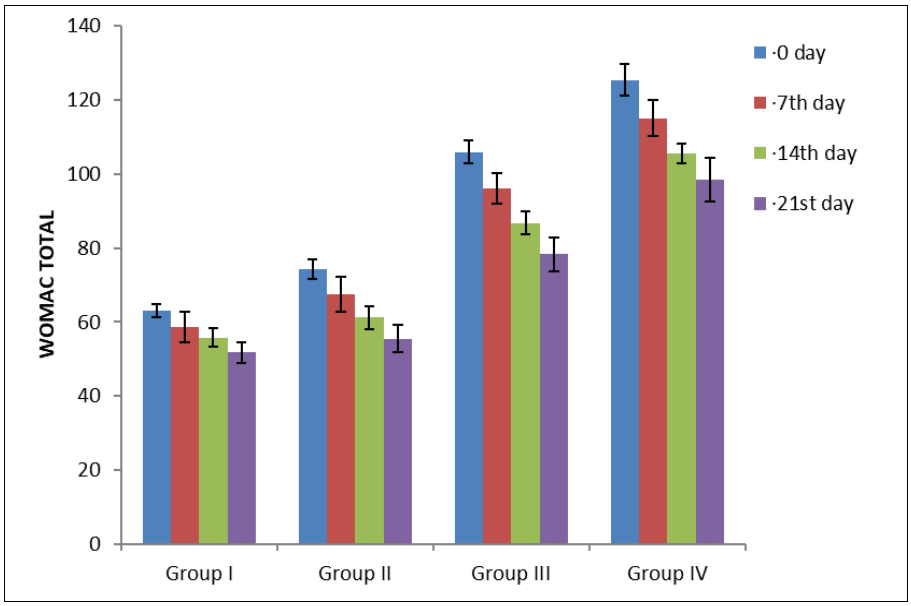
6. **Past history:** Out of 60 patients participated in the study 43 (71.7%) didn't have any comorbidity, whereas 31 (21.7%) had diabetes mellitus and 4 (6.7%) had hypertension. There is no significant correlation of history of comorbid diseases with osteoarthritis.
7. **Duration of illness:** According to the duration of illness the frequency distribution of this study. Out of 60 study participants, 35(58.3%) suffered with osteoarthritis of <3 years, 11(18.3%) had duration of 9-12 years, 9(15%) had duration of 3-6 years and 5(8.3%) had duration of 6-9 years of illness.
8. It may be noted that as duration of illness is proportionately associated with grades of the disease. The shorter duration had lesser damage to knee joints, as the duration increased the wear and tear of the joint also increased. There is a significant increase in damage to the patients with duration illness. Observation of chronicity of disease was supports the claims made by Colledge *et al.* 142.
9. **Dietary Habits:** Out of 60 participants of this study 55 (91.7) % are of mixed diet and 5(8.3%) patients were vegetarian. There is no significant correlation of diet with osteoarthritis. The study conducted by SRazana MCN [14] had corroborate this finding that prevalence of Osteoarthritis knee is associated with dietary habits. A regression analysis done by Hailu A *et al* [27] reported that heavy meat consumption is associated with higher prevalence of degenerative arthritis and soft tissue disorder. There is relationship between dietary habits and precipitation of disease according to Razi [1] and Ibn Sina [7] as they have restricted non-vegetarian foods in patients of Wajaul Mafasil. Therefore, it may be inferred that nonvegetarian diet which is usually not easily digestible and affects the digestion may act as an aggravating factor for Wajaul Mafasil.
10. **Life style:** Out of 60 participants of this study 46(76.7%) patients were found with moderate type of life style, 10(16.7%) strenuous life style 4(6.7%) had sedentary life style patients.
11. Study by Chang AG *et al* [28] suggest that continuous strenuous life style prevalence is present in Osteoarthritis Knee.
12. **Socio economic status:** Out of 60 participants of this study 31(51.7%) belongs to lower middle (SES III), 26(43.3%) upper middle (SES II), 2(3.3%) upper lower (SES IV) patients and 1(1.7%) upper (SES I) were present.
13. There is no significant correlation of Socio-economic status with Osteo arthritis. This study was conducted using Modified Kuppuswamy's scale for SES.
14. **Addiction:** Out of 60 participants of this study 55(91.7%) were neither addicted to smoking nor alcohol, whereas 4(6.7%) addicted to smoking and 1(1.7%) addicted to alcohol.
15. **Family history of Osteoarthritis:** According to the family history of osteoarthritis frequency distribution of study participants. Group I, Group II, Group III and Group IV had nil family history.
16. **Mizaj:** According to the Mizaj frequency distribution of the study participants all the 60(100%) study participants of this study were of Balghami mizaj. The Unani literature also states that people of Balghami mizaj are prone for osteoarthritis. The people with Balghami temperament are more likely to develop osteoarthritis in comparison with other humours [1, 5, 6, 7] There is great significance of Balghami mizaj with Osteo arthritis. Studies conducted by, Razana MCN [14] correlate with the results.

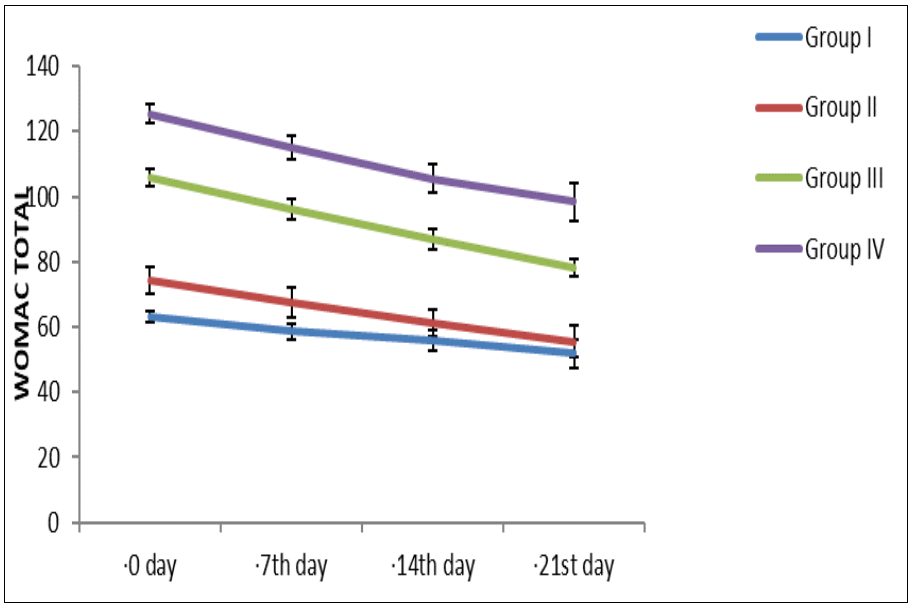
Table 1: Womac total-assessment in four groups of patients studied @ study points

Womac Total	Group I	Group II	Group III	Group IV
0 day	63.13±1.77	74.27±4.03	105.87±2.47	125.40±2.77
7th day	58.60±2.56	67.53±4.63	96.00±3.09	115.07±3.59
14th day	55.73±3.06	61.27±4.18	86.80±3.19	105.47±4.47
21st day	51.80±4.28	55.53±4.81	78.27±2.63	98.40±5.91
Difference from 0th day				
7th day	4.533	6.733	9.867	10.333
14th day	7.400	13.000	19.067	19.933
21st day	11.333	18.733	27.600	27.000
P Value From 0th Day				
7th day	<0.001**	<0.001**	<0.001**	<0.001**
14th day	<0.001**	<0.001**	<0.001**	<0.001**
21st day	<0.001**	<0.001**	<0.001**	<0.001**

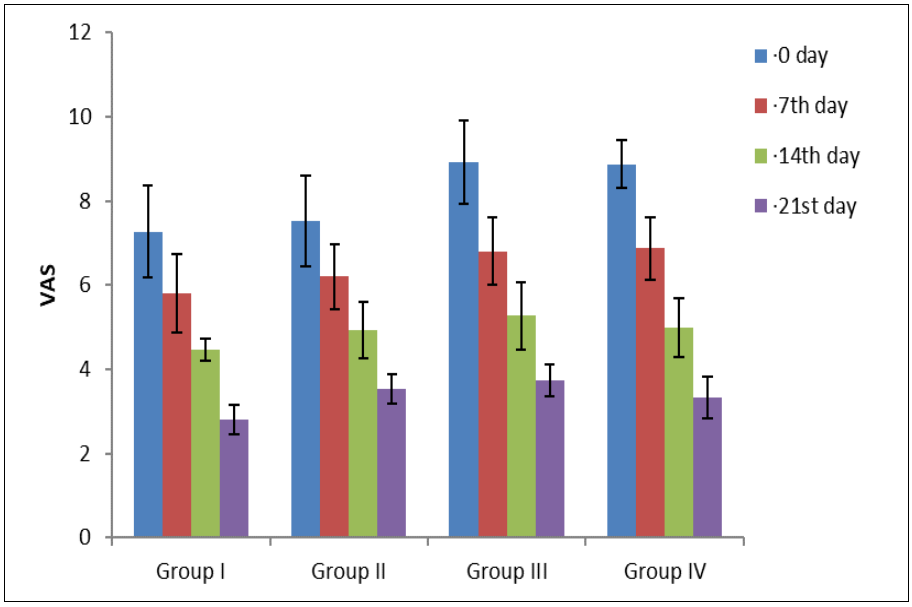
Table 2: Vas-assessment in four groups of patients studied @ study points

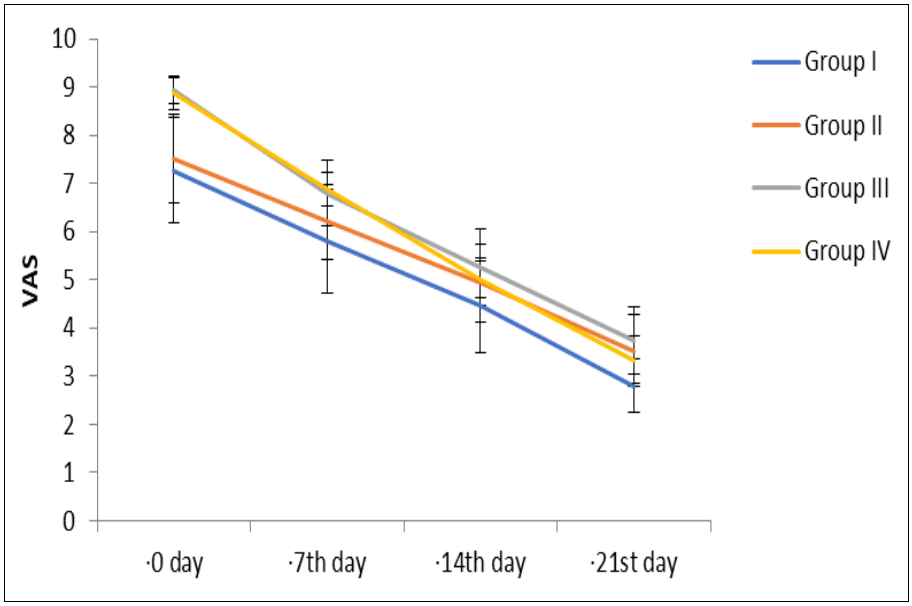
VAS	Group I	Group II	Group III	Group IV
Results				
0 day	7.27±1.10	7.53±0.92	8.93±0.26	8.87±0.35
7th day	5.80±1.08	6.20±0.77	6.80±0.68	6.87±0.35
14th day	4.47±0.99	4.93±0.80	5.27±0.80	5.00±0.38
21st day	2.80±0.56	3.53±0.74	3.73±0.70	3.33±0.49
Difference from 0th day				
7th day	1.467	1.333	2.133	2.000
14th day	2.800	2.600	3.667	3.867
21st day	4.467	4.000	5.200	5.533
P value from 0th day				
7th day	<0.001**	<0.001**	<0.001**	<0.001**
14th day	<0.001**	<0.001**	<0.001**	<0.001**
21st day	<0.001**	<0.001**	<0.001**	<0.001**





Graph 1: Showing WOMAC assessment in 4 groups based on Kellgren Lawrence Scale and intervention





Graph 2: Showing VAS assessment in 4 groups based on kellgren Lawrence scale and intervention

Conclusion

A clinical trial study was carried out to evaluate the efficacy of a Habbe Gule Aakh in osteoarthritis knee of different grades according to Kellgren Lawrence scale of osteo arthritis knee, with different doses of HGA.

The observation of the study reveals that Habbe Gule Aakh orally in dose of 500mg for group (grade) I, 1000 mg for group (grade) II, 1500 mg for group (grade) III and 2000 mg for group (grade) IV for a period 21 days shows significant improvement (p<0.001) in patients of all groups with objective parameters of WOMAC (modified) Pune Questionnaire and VAS without any adverse effects.

The strength of the study lies in dose escalation of Habbe Gule Aakh. Use of WOMAC (Modified) CRD Pune Questionnaire and VAS scale. Efficacy assessment done on subsets of symptoms.

The limitations inherent to this study include. Short duration of treatment. No follow up after completion of trial. Correction of degeneration is not studied. Control not used as it is an established drug in management of osteoarthritis.

Hence further studies are imperative to obtain more evidence know safety of Habbe Gule Aakh are required. Post treatment follow-up should be done

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Conflict of Interest:

Not available

Financial Support:

Not available

References

1. Razi Z. Kitab-al-Hawi Fit Tibb (Urdu translation), CCRUM, and New Delhi. 2004;(11):75-188.
2. Richmond J, Hunter D, Irrgang J, Jones AM, Snyder-Mackler L, Daniel Van Durme MD, *et al*. The treatment of osteoarthritis (OA) of the knee. J Bone Joint Surg Am. 2010;92:990-993.
3. Murray CJ, Lopez AD, World Health Organization. The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020: Summary: 25. World Health Organization; c1996.
4. Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. Bulletin of the world health organization. 2003 Sep;81(9):646-656.
5. Arzani A. TibeAkbar. (Urdu Translation by Mohammad Husain). Deoband: Faisal Publications, YNM. p.617-28.
6. Ismail Jurjani. Zakheera Khawarzam Shahi. (Urdu translation by Khan HH).Vol. 2. Part 6th. New Delhi: Idara Kitabus Shifa; c2010. p.637-40.
7. Ibn Sina. Al Qanoon fit Tib. (Urdu translation by Kantoori GH). Vol. 3. Part 2. New Delhi: Idarakitabus Shifa; YNM. p. 1119-21, 1129 p.
8. Nayab M. An Overview of Waja-ur-Rukbah (Knee Osteoarthritis) with Reference to Waja-ul-Mafasil and its Regimenal Management (Ilaj Bit Tadbeer) in Unani System of Medicine. Asian Journal of Traditional, Complementary and Alternative Medicines. 2021 Apr 1;4(12):19-29.
9. Kabiruddin. Al-Qarabadeen. 3rd Ed. New Delhi: CCRUM; c2006. p. 183-186, 466-468, 1210-1215.
10. Kabiruddin. Bayaze Kabeer. New Dehli: Idarae Kitabus shifa; c2010. p.30,37,50,57,88,94,176, 177, 179, 80,89-93.
11. Felson DT, Lawrence RC, Dieppe PA, Hirsch R, Helmick CG, Jordan JM, *et al.* Osteoarthritis: new insights. Part 1: the disease and its risk factors. Annals of internal medicine. 2000 Oct 17;133(8):635-646.
12. Ganga B, Wadud A, Jahan N, Makbul SA. Anti-inflammatory and analgesic activity of Habbe Gule Aakh, A polyherbal Unani formulation in animal models. Journal of Ayurveda and Integrative Medicine. 2021 Jan 1;12(1):9-12.
13. Baig MG, Quamri MA. A randomized open labeled comparative clinical study on the efficacies of Hijamat Bila Shurt and Habbe Gule Aakh in cervical spondylosis. International Journal of Current Research and Review. 2015 Jan 15;7(2):41.
14. Razana MC, Quamri MA. A randomized comparative clinical study on osteoarthritis knee with Unani formulations (Oral and Local) and Hijama Bila Shart.

15. Wewers ME, Lowe NK. A critical review of visual analogue scales in the measurement of clinical phenomena. Research in Nursing and Health 1990;13:227-236.
16. Roos EM, Roos HP, Lohmander LS. WOMAC Osteoarthritis Index-additional dimensions for use in subjects with post-traumatic osteoarthritis of the knee. Osteoarthritis and Cartilage. 1999 Mar 1;7(2):216-221.
17. Roos EM, Toksvig-Larsen S. Knee injury and Osteoarthritis Outcome Score (KOOS)-validation and comparison to the WOMAC in total knee replacement. Health and quality of life outcomes. 2003 Dec;1(1):1-10.
18. Salaffi F, Leardini G, Canesi B, Mannoni A, Fioravanti A, Caporali RO, *et al*. Reliability and validity of the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index in Italian patients with osteoarthritis of the knee. Osteoarthritis and cartilage. 2003 Aug 1;11(8):551-60.
19. Bernard Rosner. Fundamentals of Biostatistics, 5th Edition, Duxbury; c2000. p. 80-240.
20. Robert H Riffenburg. Statistics in Medicine, second edition, Academic; c2005. p. 85-125.
21. Sunder Rao PSS, Richard J. An Introduction to Biostatistics, A manual for students in health sciences, New Delhi: Prentice hall of India. 4th Edition; c2006. p. 86-160.
22. Suresh KP, Chandrasekhar S. Sample Size estimation and Power analysis for Clinical research studies. Journal Human Reproduction Science. 2012;5(1):7-13.
23. IBM Corp. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp; c2013.
24. Nagashima H, Suzuki M, Araki S, Yamabe T, Muto C, Tanezumab Investigators. Preliminary assessment of the safety and efficacy of tanezumab in Japanese patients with moderate to severe osteoarthritis of the knee: A randomized, double-blind, dose-escalation, placebo-controlled study. Osteoarthritis and cartilage. 2011 Dec 1;19(12):1405-412.
25. Munjal YP, Sharm SK. API textbook of medicine, two volume set. JP Medical Ltd; c2012 May 18.
26. Kasper DL, Fauci AS, Longo DL, Braunwald E, Hauser SL, Jameson JL. Harrison's Principles of Internal Medicine. 20th Edition. United States: MC Graw Hill; 2018;2:2625-2631.
27. Hailu A, Knutsen SF, Fraser GE. Associations between meat consumption and the prevalence of degenerative arthritis and soft tissue disorders in the Adventist health study, California USA. The Journal of Nutrition, Health & Aging. 2006;10(1):7.
28. Cheng Y, Macera CA, Davis DR, Ainsworth BE, Troped PJ, Blair SN. Physical activity and self-reported, physician-diagnosed osteoarthritis is physical activity a risk factor?. Journal of clinical epidemiology. 2000 Mar 1;53(3):315-322.

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