Efficacy of Qai, Munzij wa Mus'hil-e-Balgham and Dalk with Roghan-e-Chobchini in Waja-ur-Rukba (Knee Osteoarthritis)

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ABSTRACT: Osteoarthritis is the commonest of all joint diseases and knee is the commonest of the large joints affected by Osteoarthritis. It results due to breakdown and destruction of joint tissues. The present study was designed to evaluate the Efficacy of Qai, Munzij wa Mus'hil-e-Balgham and Dalk with Roghan-e-Chobchini in Waja-ur-Rukba (Knee Osteoarthritis). It was an open labelled, pre and post clinical study carried out on 30 patients of knee osteoarthritis at NIUM Hospital, Bengaluru. After taking written voluntary informed consent, Qai was induced on the 1st day. From 2nd day onwards, Joshanda Munzij-e-Balgham was given once in the morning till 15th day. Ingredients of Joshanda Mus'hil-e-Balgham were mixed with those of Munzij-e-Balgham and the prepared decoction given on 13th and 15th day of treatment. From 16th day onwards, Dalk Layyin Kaseer was done with Roghan-e-Chobchini on affected joint till 30th day. Patients were assessed at baseline, 15th day and 30th day of treatment by using VAS and KOOS scales. Significant improvement was observed in objective parameters using paired t-Test. VAS was found to be strongly significant at 15th and 30th day when compared with baseline. (p <0.001) All the KOOS subscales were significant statistically at 15th and 30th day. Safety parameters were in their normal range. The study revealed that the regimen of Qai, Munzij wa Mus'hil-e-Balgham and Dalk with Roghan-e-Chobchini is safe and effective in Waja-ur-Rukba (Knee Osteoarthritis).

Keywords: Knee Osteoarthritis; Qai; Munzij; Mushil; Dalk; KOOS; VAS.

I. **Introduction:**

Osteoarthritis is the most common form of arthritis. 1 It is characterized by focal loss of cartilage, subchondral bone sclerosis and new bone formation called osteophytes. Knee osteoarthritis is the commonest form of OA.² Knee OA is a leading cause of painful ambulation and is more common in women than in men.³ It is estimated that nearly half of all adults will have symptomatic knee OA in their life. 4 90% of all people develop radiographic features of OA in weight bearing joints like knee by age 40.5 Important risk factors include obesity, female gender and knee bending. Previously, OA was considered as non inflammatory disorder. However, about 25% patients of knee OA manifest with clinical evidence of inflammation that may be secondary to release of IL-1 and the normal consequence of ageing.²

The clinical picture of knee OA strongly resembles with Waja-ul-Mafasil. According to Hakim Azam Khan, Wajaul-Mafasil is pain in joints of the body, not specific to particular joint but involves joints of hands and legs. If individual joint is affected like elbow, hip, ankle, knee or fingers, it is named like Nigris, Waja-ul-Warik, Waja-ur-Rukba etc. 6 Generally this disease is caused by weakness of the joint involved which is followed by accumulation of morbid matter into it. This morbid matter may be *Damwi*, *Balghami*, *Safrawi*, *Saudawi* or mixture of these *Akhlat*.

The current modern treatment of osteoarthritis is aimed at minimizing pain, optimizing function and reducing disability using a combination of non pharmacological, pharmacological and surgical therapies.² In view of high prevalence, side effects of pharmacological treatment and high cost of surgical interventions with less effectiveness of all treatment modalities, there is need for search of safe, economic and effective treatment in Unani system of Medicine for osteoarthritis, particularly of a knee joint. Hakim Muhammad Azam Khan in Akseer-e-Azam described treatment for Waja-ul-Mafasil Balghami. He mentioned Qai (emesis) followed by Munzij wa Mus'hil-e-Balgham in its treatment. Further, in the context of Waja-ul-Mafasil, he mentioned Dalk with Roghan-e-Chobchini.⁶

II. Material and methods:

The present clinical trial is Open, Single arm, Pre and Post clinical study carried out at the Hospital of National Institute of Unani Medicine, Bengaluru. Between June 2017 to Feb 2018. After obtaining approval from IEC, patients of knee osteoarthritis were enrolled from OPD/IPD of NIUM hospital after fulfilling the inclusion criteria.

Inclusion criteria was 40-60 years of either gender with ACR clinical and radiographic criteria. Exclusion criteria included pregnancy and lactation, systemic and metabolic diseases, knee joint pathology other than osteoarthritis, having history of trauma and accidents involving knee joints and known cases of gastric ulcer and esophageal varices. After complete history and physical examination, patients fulfilling inclusion criteria were subjected to hematological and radiological investigations. A written voluntary informed consent was obtained for the trial. Safety parameters included blood investigations such as Hb %, TLC, DLC, ESR, Blood Urea, S. Creatinine, S. Bilirubin, AST, ALT, Alkaline Phosphatase. Investigations for Diagnosis and Exclusion criteria were FBS/PPBS, CRP, RA factor, Uric acid, ASO and X-ray knee Joints (AP & Lat.).

Procedure:

The treatment was started with induction of *Qai* (emesis). *Qai* was induced with *Joshanda* for *Qai* on 1st day. To prepare decoction, *Aslussoos* and *Tukhm-e-Shibt* were boiled in 250ml of water till the initial quantity reduces to half. It was then filtered, mixed with 25gms of honey and given to drink. *Qai* was induced in afternoon as per Unani literature. Ingredients of *Munzij-e-Balgham* were administered in decoction form orally, once in the morning for 14 days, i.e. from 2nd to 15th day on empty stomach. On the 13th day, the ingredients of *Mus'hil-e-Balgham* were mixed with those of *Munzij-e-Balgham* and given in decoction form for purgation. *Mus'hil-e-Balgham* was again repeated on 15th day. From 16th day of treatment, *Dalk Layyin Kaseer* was started with 25 ml of *Roghan-e-Chobchini* on affected knee joint for 10 minutes, once daily till the 30th day.

Trial Formulation:

Ingredients of Joshanda for Qai: 6,9

Shibt (Anethum graveolens Linn) 3 gms, *Aslussoos (Glycyrrhiza glabra Linn)* 5 gms, Water 250 ml, Honey 25 gms **Ingredients of** *Joshanda Munzij-e-Balgham:* ^{6,9}

Aslussoos (Glycyrrhiza glabra Linn) 5 gms, Tukhm-e-kasni (Cichorium intybus Linn) 7 gms,

Maveez Munaqqa (Vitis vinifera Linn) 9 no. Tukhm-e-Kharpaza (Cucumis melo Linn) 7 gms,

Tukhm-e-Khatmi (Althaea officinalis Linn) 5 gms, Suranjan shireen (Colchicum autumnale Linn) 3 gms, Boozidan (Tanacetum umbelliferum Boiss) 5 gms, Anisoon (Pimpinella anisum Linn) 3 gms, Badranjboya (Melissa officinalis Linn) 5 gms, Parsiyaoshan (Adiantum capillus-veneris Linn) 5 gms, Favvah (Rubia tinctorum Linn) 3 gms.

Ingredients of *Joshanda Mus'hil-e-Balgham***:** ^{6,9}

Barg-e-Sana (Cassia angustifolia Linn) 5 gms, Turbud (Ipomoea turpethum Linn) 5 gms,

Zanjabeel (Zingiber officinale Roscoe) 1gm, Barang Kabli (Embelia ribes Burm.f.) 2 gms

Maghz Khayar Shambar (Cassia fistula Linn) 25 gms

Ingredients of *Roghan-e-Chobchini***:** ^{6,9,10}

Chobchini (Smilax china Linn) 8 gms, Barge mehndi (Lawsonia inermis Linn) 40 gms,

Suranjan Shireen (Colchicum autumnale Linn) 40 gms, Rasaut (Berberis vulgaris Linn) 40 gms, Roghan-e-Kunjad (Oil of seeds of Sesamum indicum Linn) 2.4 litre. Roghan-e-Chobchini was prepared in the NIUM pharmacy as per Qarabadeen Najmul Ghani after proper scrutiny of every ingredient by the concerned department.

Assessment of efficacy:

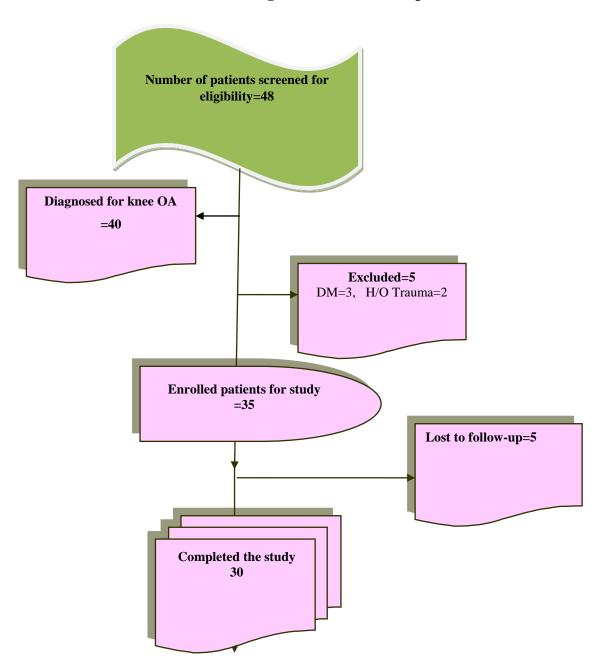
Knee osteoarthritis outcome score (KOOS) consists of 5 subscales. Pain, other symptoms, activities of daily living (ADL), sport and recreation (sports/recreation) and knee-related quality of life (QoL). Lach question was assigned a score from 0-4. A normalized score (100 indicating no symptom and 0 indicating extreme symptom) was calculated. VAS was used for evaluation of pain intensity. Follow up was carried out at 15th and 30th day of treatment.

Statistical Analysis: 14,15,16

Descriptive and inferential statistical analysis was carried out in the present study. Significance was assessed at 5% level of significance. Student *t* test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within group. The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data.

Trial Registration No: CTRI/2018/05/013978

Figure 1: Flow chart of patients studied



III. **Results:**

The baseline demographic data has been given in Table 1. All the five subscales of KOOS (knee osteoarthritis outcome score) were found to be highly significant at 15th day and 30th day of treatment. (p=<0.001)When 15th day values were compared with 30th day, highly significant improvement was observed. (p=<0.001). VAS score was also highly significant both at 15th and 30th day. No adverse events were observed throughout the trial.

Table 1 Demographics of study population

Table 1. Demographics of study population					
	No of patients	percentage			
Age					
41-50	14	46.7	Mean \pm SD:		
51-60	16	53.3	52.20±5.24		
Gender					
Female	21	70			
Male	9	30			
Religion					
Hindu	17	56.7			
Muslim	12	40			
Christian	1	3.3			
Diet					
Mixed	25	83.3			
Vegetarian	5	16.7			
Lifestyle					
Sedentary	14	46.7			
Average	13	43.3			
Labourer	3	10			
Socioeconomic					
status	1	3.3			
Lower	11	36.7			
Lower middle	3	10			
Upper	5	16.7			
Upper middle	10	33.3			
Upper lower					
BMI (kg/m ²)					
<18.5	0	0	Mean \pm SD:		
18.5-25	12	40	25.50±2.13		
25-30	18	60			
>30	0	0			
Joint involvement					
Both knee	28	93.3			
Left	1	3.3.			
Right	1	3.3			
Worst affected joint					
Left	13	43.3			
Right	17	56.7			

Table. 2 Right Knee Osteoarthritis Outcome Score: Assessment at Baseline, 15th day and 30th day of treatment

Knee Osteoarthritis		Results	P values (difference)			
Outcome Score: Right	Baseline	15 th day	30 th day	BL- 15 th day	BL-30 th day	15-30 th day
Symptoms	44.38±17.86	58.86±13.77	69.07±12.36	<0.001** (14.48)	<0.001** (24.68)	<0.001** (10.20)
Pain	37.83±18.09	53.90±15.78	66.83±13.56	<0.001** (16.06)	<0.001** (29.0)	<0.001** (12.93)
ADL	41.00±17.06	54.14±17.09	64.31±16.20	<0.001** (13.14)	<0.001** (23.31)	<0.001** (10.17)
Sport & Recreation	32.24±16.93	51.21±11.39	63.28±11.28	<0.001** (18.97)	<0.001** (31.03)	<0.001** (12.07)

Student *t* test (Two tailed, Paired)

Table. 3

Left Knee Osteoarthritis Outcome Score: Assessment at Baseline, 15th day and 30th day of treatment

Knee Osteoarthriti		Results	P values (difference)			
s Outcome Score: Left	Baseline	15 th day	30 th day	BL- 15 th day	BL-30 th day	15-30 th day
Symptoms	46.66±16.6 5	60.83±13.1	71.00±11.0 7	<0.001* * (14.17)	<0.001* * (24.34)	<0.001* * (10.17)
Pain	38.79±19.2 5	54.48±17.1 9	67.76±14.2 0	<0.001* * (15.68)	<0.001* * (28.96)	<0.001* * (13.27)
ADL	41.31±17.0 7	54.14±15.1 4	66.00±14.4 8	<0.001* * (12.87)	<0.001* * (24.69)	<0.001* * (11.87)
Sport & Recreation	33.28±18.6 3	50.34±15.1 7	63.45±12.3	<0.001* * (17.08)	<0.001* * (30.17)	<0.001* * (13.10)

Student *t* test (Two tailed, Paired)

Table. 4 Knee Osteoarthritis Outcome Score: Assessment of Quality of Life (QoL)

Knee Osteoarthriti	Results			P values (difference)		
s Outcome Score	Baseline	15 th day	30 th day	BL- 15 th day	BL-30 th day	15-30 th day
QoL	24.93±13.6 8	42.67±12.7 4	59.30±12.9 4	<0.001* * (- 17.733)	<0.001* * (- 34.367)	<0.001* * (-16.63)

Table. 5 Assessment of VAS score at Baseline, 15th day and 30th day of treatment

VAS:		Results		P values (difference)		
Pain intensity	Baseline	15 th day	30 th day	BL- 15 th day	BL-30 th day	15-30 th day
Right	6.86±1.48	4.97±1.30	3.45±1.40	<0.001** (1.89)	<0.001** (3.42)	<0.001** (1.52)
Left	6.79±1.50	4.79±1.21	3.17±1.10	<0.001** (2.00)	<0.001** (3.62)	<0.001** (1.62)

Table. 6

Assessment of safety parameters before and after treatment

Assessment of safety parameters before and after treatment								
variables	Before Treatment	After Treatment	Differenc e	t value	P value			
Hemoglobin (g/dl)	12.24±1.84	12.38±2.13	-0.137	0.699	0.490			
TLC	5643.33±1642.8 9	5938.33±1859.6 3	-295.000	0.689	0.496			
Polymorphs	62.03±8.72	62.43±8.22	-0.400	0.179	0.859			
Lymphocytes	28.23±8.05	28.83±8.87	-0.600	-0.260	0.796			
Eosinophils	5.17±1.15	4.40±1.63	0.767	2.392	0.023*			
Monocytes	4.57±1.30	4.00±1.72	0.567	1.831	0.077+			
Basophils	0.00 ± 0.00	0.00±0.00	-	-	1			
Erythrocyte sedimentation rate	37.73±19.89	27.47±18.61	10.267	3.117	0.004**			
Blood Urea (mg/dl)	25.43±4.44	27.67±4.99	-2.233	3.021	0.005**			
Serum Creatinine (mg/dl)	0.76±0.13	0.79±0.13	-0.033	1.355	0.186			
Aspartate Aminotranferas e	19.60±7.76	23.00±8.90	-3.400	2.121	0.043*			
Alanine Aminotranferas e	22.07±6.95	24.27±9.73	-2.200	1.324	0.196			
Alkaline Phosphatase	242.40±69.73	234.10±63.18	8.300	0.934	0.358			
Bilirubin	0.57±0.25	0.55±0.26	6.297	23.01	<0.001*			

Student t test (Two tailed, Paired)

IV. **Discussion:**

The study was conducted to evaluate the efficacy of Qai, Munzij wa Mus'hil-e-Balgham and Dalk with Roghan-e-Chobchini in Waja-ur-Rukba. Out of 30 patients, 14 (46.7%) patients were from age group 41-50 years and 16 (53.3%) from age group 51-60 years. (Table.1) It infers that number of patients with knee OA increased with increase in age. The increase in the prevalence and incidence of OA with age is probably a consequence of cumulative exposure to various risk factors and biological changes that occur with ageing that make a joint less able to cope with adversity, such as cartilage thinning, weak muscle strength, poor proprioception and oxidative damage. 17 Out of 30 patients, 21 (70%) patients were female and 9 (30%) patients were male, (Table.1) which is in conformity with study of Barbara *et al.*¹⁸ The definite increase in OA in women around the time of menopause are probably due to hormonal factors.¹⁷ Out of 30 patients, 12 (40%) patients had normal BMI. On the other hand, 18 (60%) patients were overweight. This result is consistent with study of Ja ryholm et al., Stürmer T et al and Sandmark et al. 19,20 There is almost doubling of risk of knee OA with increase in BMI of 5kg/m². 19 Regarding dietary habits, out of 30, 25 (83.3%) patients were of mixed dietary pattern while 5 (16.7%) were vegetarian. (Table.1) Unani Physicians have advised restriction of non-vegetarian foods in Waja-ul-Mafasil. 21,22 Incidence of OA was more in patients with sedentary lifestyle. Out of 30 patients, 14 (46.7%) were having sedentary lifestyle. (Table.1) It is in consonance with Pal CP et al.²³ Eminent Unani Physicians also have stated that physical inactivity may cause Waja-ul-Mafasil.^{7,21} Out of 30 patients, 28 (93.3%) patients had involvement of both knee joints. (Table.1) This finding coincides with Khalid M et al.²⁴ and MA Shakoor et al.²⁵ which show that most of the study subjects had bilateral involvement of knee. Studies have reported that knee OA is more common in bilateral knees.²⁶ Studies have shown that the biomechanics of unaffected knee is not normal in patients with unilateral knee osteoarthritis and also gait asymmetries exist that subsequently may change in bilateral involvement.²⁷ 17 (56.7%) patients were having right knee affected much severely than the left knee, (Table.1) which is consistent with Hawamdeh ZM *et al.*²⁸ MA Shakoor *et al.*²⁵ Sernert N *et al.*, who reported that KT 1000 arthrometer showed a significant increase in laxity measurements in right knee as compared to left knee.²⁹ that may be probable mechanism of more involvement of right knee in OA.

All the five subscales of Knee Osteoarthritis Outcome Score were found to be highly significant (p < 0.001) when baseline values were compared to those of 15^{th} and 30^{th} day. When score of 15^{th} day was compared with 30^{th} day, it was also strongly significant. (p < 0.001) (Table.2,3&4)

The VAS score of both knee joints was found to be strongly significant (p < 0.001) when comparison was made at 15^{th} day and 30^{th} day with respect to base line values. When VAS score of 15^{th} day was compared with 30^{th} day, it was also strongly significant. (p < 0.001) (Table.5)

The causes, clinical features and treatment of *Waja-ur-Rukba* is same as that of *Waja-ul-Mafasil*. and *Waja-ul-Mafasil* occurs mostly due to *Balghami Khilt*. Sign and symptoms of knee osteoarthritis resemble that of *Waja-ur-Rukba*, hence *Usool-e-Ilaj* of *Waja-ul-Mafasil Balghami* was followed in the present study. In the diseases which are caused by morbid *Akhlat*, *Tanqiya* or *Istefragh* of that particular *Khilt* is necessary. In this study *Tanqiya* was done in the form of *Qai*, followed by *Munzij wa Mus'hil* drugs. After purging out *Akhlate Raddiyah* from the diseased organ, restoration of normal temperament of that organ is necessary, which is called *Ta'deele Mizaj*. *Ta'deele Mizaj* is brought about either by drugs or regimens like *Dalk* and *Riyazat* etc. In the present study, it was achieved by *Dalk* with *Roghan-e-Chobchini*.

Qai was induced by *Joshanda* of *Tukhm-e-Shibt* and *Aslussoos* mixed with honey. All these drugs are categorized as weak emetics as per Unani literature. The ingredients of *Joshanda Munzij-e-Balgham* used in the trial possess varied actions such as *Muhallil, Mulattif, Mufatteh* etc. *Aslussoos* is *Munzije Akhlat-e-Murakkab*, Nervine tonic Amusakkin, *Muqawwi* and *Mudirre Baul wa Haiz* It has strong Anti-inflammatory activity exhibited by reducing nitric oxide and prostaglandin E2 production in the LPS-stimulated mouse macrophage cell. It also inhibits the production of pro-inflammatory cytokines. *Tukhm-e-Kasni* is *Musakkine Safra wa Khoon, Mufatteh Sudad* Mudire Baul And Dafa-e-Humma TNF-α mediated induction of COX-2 expression was suppressed by the chicory extract. This indicates its anti-inflammatory property.

Maveez Munaqqa has Munzije Khilte Ghaleez, 32,9,36 Mufatteh Sudad, Muhallil, 32,9 Muqavvie Jigar, 32 Musammine Badan and Munaffise Balgham actions. The chemical constituents present in Vitis vinifera namely Quercetin, Galactoside and Glucuronide exhibited decreased density of TNF-α immunoreactive cells and inhibited vascular permeability induced by acetic acid in rats. They also inhibited COX 1 and COX 2.38

Tukhm-e-Kharpaza is *Murattib*, *Mufarreh Qalb wa Dimagh*, *Jali*, *Mulayyin*⁹ and *Mudir*⁹ *Cucumis melo* is well known for its Antioxidant effect and antioxidants are protective molecules associated with lower risk of degenerative disease.³⁹

Tukhm-e-Khatmi has got *Muhallil, Munaffis-e-Balgham, Rade, Murakhkhi* and *Munzij*. ⁴⁰properties. Hypolaetin 8-glucoside found in *Tukhme Khatmi* has been tested for its Anti-inflammatory, Analgesic and Anti-ulcer activity in rats. ⁴¹

Suranjan Shireen is an important drug as far as joint disorders are concerned. As per Unani texts, it has Mus'hil-e-Balgham, Muhallil-e-Awram and Musakkin-e-Awram^{32,9} properties. Colchicum autumnale is rich in alkaloids especially Colchicine. Many studies showed that it has Antitumoral and Anti-inflammatory activity.⁴²

Boozidan is having properties of *Muqawwi-e-Bah* and *Munaqqie Aasab wa Mafasil.* It is useful in *Waja-ul-Mafasil* and *Niqris* Study has shown its Antioxidant, Analgesic and Antimicrobial activities and thus useful in arthritis like conditions.

Anisoon is *Muhallil*, ⁴⁴ *Musakkin Auja*, *Mudir-e-Baul wa Haiz* and *Munaffis-e-Balgham*. ³³ In one of studies, essential oil of *Pimpinella anisum* showed significant Analgesic effect similar to Morphine and Aspirin. ⁴⁵

Badranjboya has got *Muqawwi-e-Qalb*, *Munzij-e-Sauda* and *Muhallil*³³ properties. The Anti-inflammatory and Anti-nociceptive effect of *Badranjboya* is due to Rosmarinic acid, Flavonoids and Terpenoids present in the extract.⁴⁶

According to Unani literature, *Parsiyaoshan* is *Munzij*, *Mus'hil-e-Balgham wa Sauda*, *Muhallil*, *Mulattif* and *Mudire Baul wa Haiz*.⁴⁷ So it can evacuate the morbific *Balgham* after altering its consistency. It contains Flavonoids and according to some findings, flavonoids possess properties of Anti-inflammatory, Antitumor and Antiosteoporotic effects.⁴⁸ *Favvah* is *Mudirr-e-Baul wa Haiz*, *Munaqqi-e-Jigar wa Tihal*, *Mufatteh Sudad*, *Musakkhin* and *Jali*.⁴⁹ Physcion and emodin, chemical constituents found in *Favvah* caused 65–68% reduction of oedema which validated their in-vivo Anti-inflammatory effect.⁵⁰

Constituents in *Mus'hil-e-Balgham* are *Barg-e-Sana*, *Turbud*, *Zanjabeel*, *Barang Kabli* and *Khayar Shambar*. *Barg-e-Sana* is *Mulayyin wa Mus'hil*, *Munaqqi-e-Dimagh*, *Mufatteh Sudad* and *Musaffi-e-Dam*.³⁴ Leaves of *Sana Makki* constitute Flavonoids which have Antioxidative properties.⁵¹

Turbud has *Mus'hil-e-Balgham* and *Munaqqi-e-Dimagh*⁴⁰ properties. According to scientific studies, it has got Anti-inflammatory, ^{52,53} Ulcer protective, ⁵³ Anti-bacterial ⁵³ and Antioxidant ^{52,53} actions.

Zanjabeel has Munaffis-e-Balgham, Kasir-e-Riyah and Jali ³⁴ actions. Zingiber species inhibit LPS-induced PGE₂ and TNF-α production. Gingerols are most active Anti-inflammatory components.⁵⁴

Barang Kabli is *Qatil-e-Deedan-e-Ama* and *Mus'hil*³⁴ in nature. It exhibits Analgesic, Amylase and Trypsin inhibitory, Antibacterial, Antioxidant etc. activities.⁵⁵

Maghz-e-Faloos Khayar Shambar is Mus'hil and Muhallil-e-Warm^{34,47} According to phytochemistry screening, it has got Anti-inflammatory activity in rats.⁵⁶

In the present study, Dalk was done by *Roghan-e-Chobchini*. Contents of *Roghan-e-Chobchini* are *Chobchini*, *Barg-e-Mehndi*, *Suranjan*, *Rasaut and Kunjad Siyah*. *Chobchini* is *Mulattif*, *Muarriq*, *Muharrik*, *Musaffi-e-Dam and Muqawwi*^{36,40} in actions. Sieboldogenin is a potential Anti-inflammatory compound responsible for Anti-inflammatory activities of *Smilax china* Linn.⁵⁷ *Barg-e-Mehndi* has got *Muhallile Awram*, *Mudire Baul* and *Munaffis-e-Balgham*³⁶ properties. Pharmacological studies reveal that it has Antidiabetic, Hepatoprotective, Antioxidant, Analgesic and Anti-inflammatory activities.⁵⁸

Rasaut has *Muhallil-e-Awram*⁵⁹ action. Bereberine and other similar alkaloids have been identified to possess diverse medicinal properties like Antimicrobial, Antiemetic, Antipyretic, Antioxidant, Anti-inflammatory, Anti-arrhythmic, Sedative, Anti-cholinergic etc.⁶⁰

Kunjad siyah is Mulayyin and Muhallile Awram⁵⁹ The oil has wide medicinal and pharmaceutical applications. It resolves inflammation.⁵⁹

Hence, the aforementioned properties of various ingredients of the test formulation strongly suggest having the potential to treat the sign and symptoms of *Waja-ur-Rukba* and their efficacy was validated in the trial.

Hematological investigations done before and after the treatment proved safety of the drugs. Significant changes were found in Eosinophils, Monocytes, ESR, Blood Urea, Aspartate Aminotranferase and Serum Bilirubin. However, these changes were within normal range.

V. Conclusion:

It can be concluded that the present study entitled "Efficacy of *Qai*, *Munzij wa Mus'hil-e-Balgham* and *Dalk* with *Roghan-e-Chobchini* in *Waja-ur-Rukba* (knee osteoarthritis)" was found to be safe and effective. The limitation of study was smaller sample size and short duration of therapy. Hence, controlled clinical trials with large sample size are required to further prove the efficacy and safety of this treatment regimen.

ACKNOWLEDGMENT

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VI. References:

- 1. Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J. Harrison's Principles of Internal Medicine. Vol.2. 18th ed. New York: Mc Graw-Hill Companies; 2012: p2828
- 2. Munjal YP, Sharma SK, Shah SN, Agarwal AK, Handa R, Das SK, *et al.* API Textbook of Medicine. Vol 2. 9th ed. Mumbai: The Association of Physicians of India; 2012: p1818-1821.
- 3. Goldman L, Schafer AI. Goldman's Cecil Medicine. 24th ed. Philadelphia: Elsevier Saunders; 2012: p1672-1676
- 4. Murphy L, Schwartz TA, Helmick CG, Renner JB, Tudor G, Koch G, *et al.* Lifetime risk of symptomatic knee osteoarthritis. Arthritis Rheum. 2008 Sep; 59:1207-13.
- 5. Papadakis MA, McPhee SJ, Rabow MW. Current Medical Diagnosis and Treatment. 54th ed. New York: McGraw Hill Education; 2015: p809
- 6. Khan MA. Akseer-e-Azam (Al Akseer). (Urdu translation by Mohd. Kabeeruddin). New Delhi: Idara Kitabus shifa; 2011: p836-849
- 7. Arzani A. Tibb-e-Akbar. Deoband: Faisal Publications; YNM: p617-18
- 8. Firestein GS, Budd RC, Gabriel SE, McInnes IB, O'Dell JR. Kelley's Textbook of Rheumatology. Vol 2. 9th ed. Elsevier Saunders; 2013: p1636-38
- 9. Kabiruddin HM. Makhzanul Mufradat. New Delhi: Idara Kitabul Shifa; 2007: p78,87,96,101,117,133,154,155,211,264,270,271,272,303,390,396
- 10. Ghani N. Qarabadeen Najmul Ghani. New Delhi: CCRUM; 2010: p495
- 11. http://www.biomedcentral.com/content/supplementary/1471-2474-7-38-s1.pdf (cited on 24.2.2017)
- 12. http://www.koos.nu/. (cited on 24.2.2017)
- 13. Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstad L, Breivik-Hals EK, *et al.* Assessment of Pain. British Journal of Anaesthesia, 2008 May; 101(1): p17-24

- 4. Rosner B. Fundamentals of Biostatistics. 5th ed. Duxbary: 2000: p80-240
- 15. Riffenburg RH. Statistics in Medicine. 2nd ed. Academic Press; 2005: p85-125
- 16. Suresh KP, Chandrasekhar S. Sample Size estimation and Power analysis for Clinical Research Studies. Journal Human Reproduction Science. 2012: 5(1), p7-13.
- 17. Zhang Y, Jordan JM. Epidemiology of Osteoarthritis. Clinical Geriatric Medicine. 2010 Aug; 26(3): 355-369
- 18. Barbara D. Boyan *et al.* Sex differences in osteoarthritis of the knee. J Am Acad Orthop Surg 2012; 20: 668-669.
- 19. Järvholm B, Lewold S, Malchau H, Vingård E. Age, bodyweight, smoking habits and the risk of severe osteoarthritis in the hip and knee in men. European Journal of Epidemiology. 2005 Jun 1; 20(6): 537-4
- 20. Stürmer T, Günther KP, Brenner H. Obesity, overweight and patterns of osteoarthritis: the Ulm Osteoarthritis Study. Journal of Clinical Epidemiology. 2000 Mar 1; 53(3): 307-13.
- 21. Majoosi A. Kamilus sana'a. (Urdu translation by GH Kanturi). New Delhi: Idara Kitabus Shifa; 2010: p190-194,503-513.
- 22. Razi ABMBZ. Kitab-ul-Hawi. Vol 11th. New Delhi: CCRUM; 2004: p75,76.
- 23. Pal CP, Singh P, Chaturvedi S, Pruthi KK, Vij A. Epidemiology Of Knee osteoarthritis in India and related factors. <u>Indian J Orthop</u>. 2016 Sep; 50(5): 518–522.
- 24. Khalid M, Siddiqui MA, Mand D, Jafar M. Clinical evaluation of Majoon Yahya Bin Khalid and Local application of Roghan Darchini in management of primary knee osteoarthritis. Journal of Biological and Scientific Opinion. 2015 December; 3(6).
- 25. Shakoor MA, Taslim MA, Ahmed MS, Hasan SA. Clinical profile of patients with Osteoarthritis of the knee: A study of 162 cases. IJPMR. 2009; 20(2): 44-7.
- 26. Metcalfe AJ, Andersson ML, Goodfellow R, Thorstensson CA. Is knee osteoarthritis a symmetrical disease? Analysis of a 12 year prospective cohort study. BMC musculoskeletal disorders. 2012 Dec; 13(1): 153.
- 27. Creaby MW, Bennell KL, Hunt MA. Gait differs between unilateral and bilateral knee osteoarthritis. Arch Phys Med Rehabil 2012; 93: 822–827.
- 28. Hawamdeh ZM, Al-Ajlouni JM. The clinical pattern of knee osteoarthritis in Jordan: a hospital based study. International Journal of Medical Sciences. 2013; 10(6): 790.
- 29. Sernert N, Ejerhed L, ón Karlsson J. Right and left knee laxity measurements: a prospective study of patients with anterior cruciate ligament injuries and normal control subjects. Arthroscopy. 2004 Jul 1; 20(6): 564-71.
- 30. Qarshi MH. Jamiul Hikmat. New Delhi: Idara Kitab-us-shifa; 2011: p247-251
- 31. Razi AMBZ. Kitabul Murshid (Urdu translation by Raziul Islam Nadvi). New Delhi: Taraqqi Urdu Bureau; 2000: p59-61
- 32. Ghani N. Khazayin-ul-Adviya. New Delhi: Idara Kitabbush-Shifa; 2010.
- 33. Anonymous. Standardization of Single Drugs of Unani Medicine. 1st ed. Part 5. New Delhi: CCRUM; 2006: p6,11,16,21,214,232.
- 34. Anonymous. The Unani Pharmacopoeia of India. Part 1. Vol 1. New Delhi: CCRUM; 2007: p9,19,54,76,88.
- 35. Assessment report on Glycyrrhiza glabra L. and/or Glycyrrhiza inflate Bat. And/or Glycyrrhiza uralensis Fisch. Europe: 12 March 2013. Report no.: EMA/HMPC/571122/2010
- 36. Anonymous. Standardization of Single Drugs of Unani Medicine. Part-1. New Delhi: CCRUM; 1987: p42,109,156,166,215,267
- 37. Street RA, Sidana J, Prinsloo G. Cichorium intybus: traditional uses, Phytochemistry, Pharmacology, and Toxicology. Evidence-Based Complementary and Alternative Medicine. 2013.
- 38. Handoussa H, Hanafi R, Eddiasty I, El-Gendy M, El Khatib A, Linscheid M *et al.* Anti-inflammatory and cytotoxic activities of dietary phenolics isolated from Corchorus olitorius and Vitis vinifera. Journal of Functional Foods. 2013 Jul 1; 5(3): 1204-16.
- 39. Sahithi G, Vasanthi R, Banji D, Rao KN, Selvakumar D. Study of phytochemical and antioxidant activity of Cucumis melo var. agrestis fruit. Journal of Pharmacognosy and Phytochemistry. 2015 Jul 1; 4(2).
- 40. Anonymous. The Unani Pharmacopoeia of India. Part 1. Vol 5. New Delhi: CCRUM; 2008: p 23,94,99,105
- 41. Al-Snafi AE. The pharmaceutical importance of Althaea officinalis and Althaea rosea: A review. Int J Pharm Tech Res. 2013; 5(3): 1387-5.
- 42. Toplan GG, Gürer C, Afife M. Importance of Colchicum species in modern therapy and its significance in Turkey. J. Fac. Pharm. 2016; 46(2): p129-144
- 43. Sujatha S, Prakash G, Vinayak K. Exploration of Bioactive Screening against the Microbial Organisms from the two different Chrysanthemum Medicinal Plant Flower with two Assorted Extracts. International Journal of Pharmacy and Bio-Sciences. 2015 Feb; 24
- 44. Baitar I. Al-Jameul Mufradat Al-Advia wal Aghzia-1 New Delhi: CCRUM; YNM
- 45. Shojaii A, Abdollahi Fard M. Review of Pharmacological properties and chemical constituents of Pimpinella anisum. ISRN Pharmaceutics. 2012 Jul 16; 2012.

- 46. Zarei A, Ashtiyani SC, Taheri S, Hosseini N. A Brief overview of the effects of Melissa officinalis L. on the functions of various body organs. Zahedan Journal of Research in Medical Sciences. 2015 Sept; (15)
- 47. Anonymous. Standardization of Single Drugs of Unani Medicine. Part 2. New Delhi: CCRUM; 1992: p211,240.
- 48. Jiang et al. In vitro and in vivo studies of antioxidant activities of flavonoids from Adiantum capillus-veneris. L. African Journal of Pharmacy and Pharmacology. 2011; 5(18): 2079-2085.
- 49. Anonymous. The Unani Pharmacopoeia of India. Part 1. Vol 4. New Delhi: CCRUM; 2007: p63,89,96.
- 50. Ghosh S, Das Sarma M, Patra A, Hazra B. Anti-inflammatory and anticancer compounds isolated from Ventilago madraspatana Gaertn., Rubia cordifolia Linn. and Lantana camara Linn. Journal of Pharmacy and Pharmacology. 2010 Sep 1; 62(9): 1158-66.
- Laghari AQ, Memon S, Nelofar A, Laghari AH. Extraction, identification and antioxidative properties of the flavonoid-rich fractions from leaves and flowers of Cassia angustifolia. American Journal of Analytical Chemistry. 2011 Dec 1; 2(08): 871.
- 52. Sharma V, Singh M. In vitro radical scavenging activity and phytochemical screening for evaluation of the antioxidant potential of Operculina turpethum root extract. J Pharm Res. 2012 Feb; 5: 783-7.
- 53. Khare Indian Medicinal Plants. 1st ed. New York: Springer; 2007: p19,20,51,88,89,127,146,147,181,289,290,406,486,487,559,599,711,712,733
- Jiang H, Xie Z, Koo HJ, McLaughlin SP, Timmermann BN, Gang DR. Metabolic profiling and phylogenetic analysis of medicinal Zingiber species: Tools for authentication of ginger (Zingiber officinale Rosc.). Phytochemistry. 2006 Aug 1; 67(15): 1673-85.
- Ram HA, Sriwastava NK, Makhija IK, Shreedhara CS. Anti-inflammatory activity of Ajmodadi Churna extract 55. against acute inflammation in rats. Journal of Ayurveda and Integrative Medicine. 2012 Jan; 3(1): 33.
- Anwikar S, Bhitre M. Study of the synergistic anti-inflammatory activity of Solanum xanthocarpum Schrad and 56. Wendl and Cassia fistula Linn. International Journal of Ayurveda Research. 2010 Jul; 1(3): 167.
- Khan I, Nisar M, Ebad F, Nadeem S, Saeed M, Khan H, et al. Anti-inflammatory activities of Sieboldogenin 57. from Smilax china Linn.: Experimental and Computational studies. Journal of Ethnopharmacology. 2009 Jan 12; 121(1): 175-7.
- Chaudhary G, Goyal S, Poonia P. Lawsonia inermis Linnaeus: A phytopharmacological review. International 58. Journal of Pharmaceutical Sciences and Drug Research. 2010; 2(2): 91-8.
- 59. Anonymous. Standardization of Single Drugs of Unani Medicine. Part 3. New Delhi: CCRUM; 1997: p26,193,261.
- Mokhber-Dezfuli N, Saeidnia S, Gohari AR, Kurepaz-Mahmoodabadi M. Phytochemistry and pharmacology 60. of berberis species. Pharmacognosy reviews. 2014 Jan; 8(15): 8.