Clinical Evaluation of Unani Drugs *Majoon Suranjan, Safoof Suranjan* and *Raughan Suranjan* in Waja-ul-Mafasil (Rheumatoid Arthritis) (A Preliminary Study)

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Abstract

Waja-ul-Mafasil is synonomously known as Rheumatoid Arthritis (RA). It is a chronic multi- system disease that affects joints, connective tissues, muscles, tendons and fibrous tissue. It occurs in about 3% of total population in the age group of 20-50 years. Females are three times more affected than males. RA manifests as a symmetric polyarthritis associated with swelling and pain in multiple joints, often initially occurring in the joints of hands and feet. The present study was conducted to evaluate the therapeutic efficacy of Unani pharmacopoeial formulations *MajoonSuranjan, SafoofSuranjan* and *RaughanSuranjan* in the management of *Waja-ul-Mafasil*. These classical Unani drugs significantly reduce joint pain ($p<0.05$), tenderness ($p<0.05$), morning stiffness ($p<0.05$), swelling ($p<0.05$), movement of restriction ($p<0.05$), and muscular weakness ($p<0.05$). The clinical and laboratory findings after treatment have shown that the trial drugs possessed efficacy in the treatment of Waja-ul-Mafasil.

This study demonstrates pronounced anti-arthritic effects indicating that these formulations would be potent drugs for arthritis patients.

Keywords: *Waja-ul-Mafasil, Majoon Suranjan, Safoof Suranjan* and *Raughan Suranjan*, Unani pharmacopoeial formulations.

Introduction

Rheumatoid arthritis is mentioned in classical Unani literature as *'Waja-ul-Mafasil'*. It is a condition of pain or an inflammation *(Waram)* which occurs in the joints of hands and feet, knee joints and ankle joints (Majoosi,1889; Ali, 1896; Jurjani, 1903). Shaikh Bu Ali Sina (Avicenna) (980-1036 AD) mentioned that *Waja-ul-Mafasil* is caused by phlegm *(Balgham),* blood *(Dam),* yellow bile *(Safra),* and black bile *(Sauda)* in a decreasing order of frequency respectively. *Waja-ul-Mafasil* is commonly caused by accumulation of viscid phlegm *(Balgham-e-Lazij)* in the joints due to weakness of the joints *(Zof-e- Mafasil)* (Majoosi, 1889; Khan, 1939). *Madda* (substance) causing *Waja-ul- Mafasil* enters into the joints and it neither absorbed nor expels from them due to lack of power of absorption *(Quwwat-e-Jazibah)* and power of expulsion *(Quwwat-e-Dafia)* in the joints, respectively and thus, it is retained in the joints, hence the nutrients reaching the joints are not properly utilized, instead they are converted into harmful products which induce inflammatory process. Thus, the *Waja-ul-Mafasil* is developed (Jurjani, 1903), when this *Madda* (substance) is retained in the joints for a long period, its viscosity

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(Ghilzat) and viscidity *(Luzoojat)* are increased and it becomes hard *(Tahajjur-e-Mafasil* or Osteoarthritis) and the condition is incurable (Majoosi, 1889). When the *Madda* (substance) which produces *Waja-ul-Mafasil* enters into the blood and permeates the entire body system, the non-articular manifestations are developed (Majoosi, 1889; Khan, 1939).The gist of all that follows: *Waja-ul-Mafasil*: when the joints suffer by pain the condition refers to *Waja-ul-Mafasil*.

It is mentioned that when the *akhlat* like *balgham* and *safra* come under *su-i-mizaj* (abnormal state), the condition becomes prone to *Waja-ul-mafasil*. It is a chronic multisystem disease characterized by a destructive and deforming polyarthritis, mainly affecting peripheral synovial joints, usually in a symmetrical pattern and a variety of non-articular manifestations In this condition joints lose their normal architecture resulted articulation disturbances, it is a condition of *sue-tarkeeb* and *tafarruq-wa-Ittissal* respectively (McGee *et al*., 1992; Kasper *et al*., 2005; Boon *et al*., 2006).

Materials and Methods

The study was designed as an open clinical trial to evaluate the efficacy of unani pharmacopoeial formulation on twenty nine patients of Waja-ul-Mofasil. The patients were treated for a period of eighty four (84) days with regular follow-ups after fourteen (14) days of interval at RRIUM, Patna. The patients suffering from Waja-ul-Mafasil were selected by adopting clinical criteria of Rheumatoid Arthritis Revised (1988) for diagnosis by the (ARA) American Rheumtism Association (Arnett *et al*., 1988). The inclusion criteria of the cases was done on the basis of pathological and biochemistry investigations (eg. RA, CRP), radiological changes and presence of joint pain, tenderness, morning stiffness, swelling, restriction of movement & muscular weakness. However, negative cases against RA and CRP were also included in the study on the basis of presence of above signs & symptoms.

Similar, the exclusion criteria was also maintained on the basis of serious disorders in renal, liver, cardiac and abnormality in any investigation (SGOT,SGPT, and ALP, SrCreatinine, B.Urea) done at the baseline. The cases, whose abnormality in investigations were found more than >2 ½ times from the normal value, drug induced, neurological, NES (Nerve Entrapment System), joint with permanent deformities, pregnant women and lactating mothers, were excluded from the study.

After written consent, the patients were enrolled for the treatment and laboratories investigations (HB%, TLC, DLC, ESR, LFT, KFT, Urine Routine, RAfactor, CRP and X-ray of affected joint) of the patients were also conducted. The investigations were repeated after treatment. The safety of the trial drugs was evaluated clinically by monitoring adverse effects which were carefully sought out on each follow-up.

The temperament (Mizaj) of the patients was assessed as per the parameter described in unani classical literature

All the signs and symptoms were assessed on each follow-up according to the flowing gradings.

Joint Pain: (1=Barely Perceptible; 2 =Mild: Can carry out daily activities with some trouble; 3= Moderate; cannot carry out daily activities easily, 4= Severe; bed ridden.)

Tenderness: (1=Patient says it is tender, 2=Patient says it is tender and winces, 3=Patient says it is tender, winces and pulls back, 4=patient does not allow palpation.)

Morning Stiffness: (1=Up to 15 minutes, 2=15 to 30 minutes, 3=30 to 45 minutes, 4=More than 45 minutes.)

Joint Swelling/ Effusion (0=No swelling/effusion, 1=Barely perceptible, 2=Mild, 3=Moderate, 4=Severe.)

Restriction of Movement: (1= Active range of motion (Partial voluntary movement), 2=Passive range of motion (Full movement, when the joint is moved by the examiner), 3= Passive range of motion (Partial movement, when the joint is moved by the examiner) Worst affected joint, 4= No movement at all.)

Muscular Weakness: (1=Strength against gravity and added resistance, 2=Strength only against gravity, not added resistance, 3=muscular contraction occurs, but not sufficient to overcome gravity, 4=Muscular contraction with little or no movement.)

Overall response was assessed on 90-100% - Complete Relief; 60-89% - Relief; 30-59% - Partial Relief and <30% - No Relief in the Improvement of sign & symptoms of disease. No concomitant treatment was allowed during the study. The observation results were statistically analyzed.

Objective of The Study

- To assess the clinical efficacy of unani pharmacopoiel formulation,*Majoon Suranjan, Safoof Suanjan & Raughan Suranjan* for symptomatic relief in patients of *Waja-ul-Mafasil* (RA).
- To assess the safety of unani pharmacopoiel formulation *Majoon Suranjan, Safoof Suanjan & Raughan Suranjan of Waja-ul-Mafasil* (RA).

Drug doses Schedule and Mode of Administration

1. Majoon-e-Suranjan

Dose: Trial drugs Majoon Suranjan (Semi-solid form-7gram) was given orally twice a day with water after meals.

Ingredients:

Name of the ingredients	Botanical Name	Qty
Suranjan Shireen	*Colchicum autmnale*	500 gm
Sana	*Cassia angustifolia* Vahl	250 gm
Zanjabeel	*Zingiber officinale* Rosc	100 gm
Zeera Siyah	*Carum carvi* L.	100 gm
Filfil draz	*Piper longum* L.	100 gm
Asaroon	*Asarum europaeum*	100 gm
Qand Safaid	*Saccharum officinarum* L.	3.5 kgs

2. Safoof-e-Suranjan

Dose: Safoof Suranjan (powder 6gram) was given orally twice a day with water after meals.

Ingredients:

Name of the ingredients	Botanical Name	Qty
Suranjan Shireen	*Colchicum autmnale*	25 gm
Buzidan	*Pyrethrum indicum* L.	25 gm
Post-e-Halela Zard)	*Terminalia chebula* Retz	25 gm
Maghz-e-Tukhme-e-Tarbooz	*Citrullus vulgaris* Schrad	25 gm
Maghz-e-badam	*Prunus amygalus* L.	25 gm
Maghz-e-Tukhm-e-Badranjboya	*Nepeta hindostana* (Roth) Haines	25 gm
Maghz-e-Tukhm-e-khaiyar-draz	*Cucumis sativus* L.	25 gm
Kishneez Khush	*Coriandrum sativus* Roxb.	25 gm
Tukhm-e-Khashkhash	*Papaver somniferum* Linn.	25 gm
Qandsafaid	*Saccharum officinarum* L.	225 gm

3. Roghan Suranjan

Dose: Raughan Suranjan (oil form) was also applied locally on the affected joints with gentle massage till it absorbed, twice a day in the morning and at bed time.

Ingredients:

Name of the ingredients	Botanical Name	Qty
Suranjantalkh	*Colchicum luteum* Baker	50 gm
Aab-e-Karafs	*Apium graveolens* L.	50 gm
Chiraita	*Swertia chirata* Buch. -Ham	25 gm
RoghanZaitoon	*Olea europaea* L.	150 gm

Laboratory Investigations

The following pathological, biochemical and radiological investigations were carried out before (baseline) & after therapy and six follow ups during 84days treatment.

Pathological Investigations

Blood for TLC (Total Leukocyte count), DLC (Differential Leucocyte Count), RBC (Red Blood Corpuscles), Hb%, ESR (Erythrocyte Sedimentation Rate), Urine R/E, were carried out. Besides these, for diagnosis of disease and assessment of response of therapy other pathological investigations CRP (C Reactive Protein) and RA (Rheumatoid Arthritis) factor for detection of Rheumatoid Arthritis were also carried out.

Biochemical Investigation

Biochemical investigations for example LFT (Liver Function Test), SGOT (Serum Glutamic OxaloaceticTransminase), SGPT (Serum Glutamic Pyruvic Transaminase), ALP (Serum Alkaline Phosphatase, Serum Bilirubin and KFT (Kidney Function Tests) Serum Urea and serum creatinine were carried out for safety of drugs.

Radiological Investigation

Radiological examination (X- ray of the affected joints) was carried out for assessment of the results.

Clinical Toxicity Evaluation

The toxicity of trial drugs was evaluated clinically by monitoring adverse effects which were carefully sought out at each follow up.

Assessment of Efficacy

The assessment of patients was done according to the subjective parameters

(joint pain, tenderness, morning stiffness, joint swelling, restriction of movement and muscular weakness) and the objective parameters (X-ray, ESR, CRP and RA factor).

As the subjective parameters differ in severity from patients to patients and an arbitrary grading, starting from 0 to 4 was improvised for appropriate assessment and statistical evaluation to evaluate the efficacy of the procedure. The clinical assessment of the patients was carried out after every 14 days and at the completion of the protocol the laboratory as well as radiological investigations were done before and after treatment. A comparative study was done against the basal clinical findings and the findings observed during first to sixth follow-ups. The difference, if any observed, was recorded in percentage and taken as the improvement caused by the respective treatment

Follow-up Evaluation

The clinical follow-up was carried out at regular intervals from 14th day to 84th day. The laboratory as well as radiological investigations was done before and after treatment.

Statistical Analysis

Statistical analysis was restricted to only those patients, who completed the full duration of study and followed the protocol. The statistical analysis were performed by Student's paired't' test. The result were expressed as Mean ± SD. Difference are considered significant at $p<0.05$.

Results and Discussion

The result regarding to the incidence of *Waja-al-Mafasil* (Arthritis) according to the demographic data and subjective parameters are as follows:-

Table 1: Classification according to stage of chronici

Chronicity (Month)	Clinical Parameters					
	Joint Pain	Tender-ness	Morning stiffness	Joint swelling	Restriction of movement	Muscular weakness
1-2 Months	01	08	16	12	15	13
3-4 Months	17	21	01	03	01	-
5-6 Months	06	-	04	09	-	-
>6 Above	05	-	08	02	01	-
TOTAL	**29**	**29**	**29**	**26**	**17**	**13**

As shown in the table no. 1, the 16, 15, 13 and 12 patients were having morning stiffness, restriction of movement, muscular weakness and joint swelling respectively in the 1-2 month of chronicity. The maximum 21 patients were having tenderness and 17 patients had joint pain of 3-4 month of chronicity. The maximum 09 patients had joint swelling from 5-6 month of chronicity. The maximum 08 patients were having morning stiffness and 05 patients joint pain from above month of chronicity. Out of 29 patients, 08 patients were having morning stiffness more than six months of chronicity of disease, 02 patients had joint swelling, and 01 patient had restriction of movements. No tenderness and muscular weakness was found in patients having 5-6 month and more than 6 month chronicity of the disease. However, no muscular weakness was found in 3-4 months chronicity of disease.

Table 2: Showing effected joints of patients

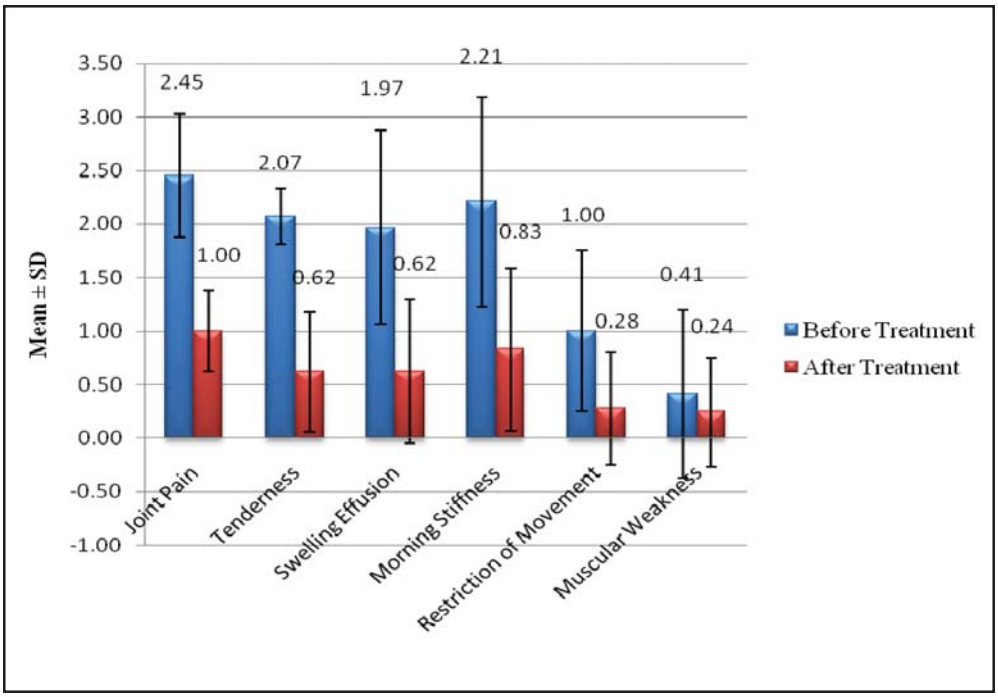
Joints Involved	Right	Left
Hip	10	–
Knee	23	21
Ankle	07	08
Shoulder	07	05
Elbow	05	03
Wrist	11	12
MCP Joints	09	06
PIP Joints	02	02
L S Joints	05	03
Cervical Joints	–	–

As shown the table no.2, maximum patients 23 & 21 were found left & right knee joints effected, next to it 11 and 12 patients were found left & right wrist joints and 1 & 2 patients were found left & right PIP joints. No patient was found to have cervical joint under the study.

As shown in the table No.3, the mean score of the joint pain before and after treatment was 2.45 and 01 which was 59% significantly. Similarly, the mean score of the tenderness before starting the treatment was 2.07 and however at the end of the treatment was 0.62. The improvement in tenderness at the end of the treatment was found 70.00%. The mean score of the swelling effusion before the treatment was measured 1.97. But at the end of treatment it was noticed was 0.62. The improvement in swelling effusion at the end of the treatment was found

Table 3: Effects of joints on subjective parameters

Parameters	Before Treatment	After Treatment	Improvement (%)
	Mean ± SD	Mean ± SD	
Joint Pain	2.45 ± 0.57	1 ± 0.38*	59.15
Tenderness	2.07 ± 0.26	0.62 ± 0.56*	70
Swelling Effusion	1.97 ± 0.91	0.62 ± 0.68*	68.42
Morning Stiffness	2.21 ± 0.98	0.83 ± 0.76*	62.5
Restriction of Movement	1 ± 0.76	0.28 ± 0.53*	72.41
Muscular Weakness	0.41 ± 0.78	0.24 ± 0.51*	41.67



68.42%. The related improvement in morning stiffness in before and after treatment was also shown. Before treatment it was 2.21 while after treatment it was 0.83. The improvement in this particular parameter was 62.50. Moreover, the mean score of the restriction of movement before and after treatment was 1 and 0.28 respectively. The improvement in restriction of movement statistically significant and it was 72.41%. And equally an improvement was also shown in muscular weakness and it was 41.67% from before and after treatment. The mean score of the muscular weakness before and after treatment was 0.41 and end of the treatment was 0.24.

Table 4: Showing response of drugs

Complete relief 90-100%	Relief 60-89%	Partial relief 30-59%	Not relieved < 30%	Total
00	20 (69%)	08 (28%)	01 (3%)	29 (100%)

Out of 29 cases, 20 (69%) patients found relief, 08 (28%) cases found partial relief and only 1 (3%) had no relief by examination of Unani classical drugs (Table No.4 and Figure No.4)

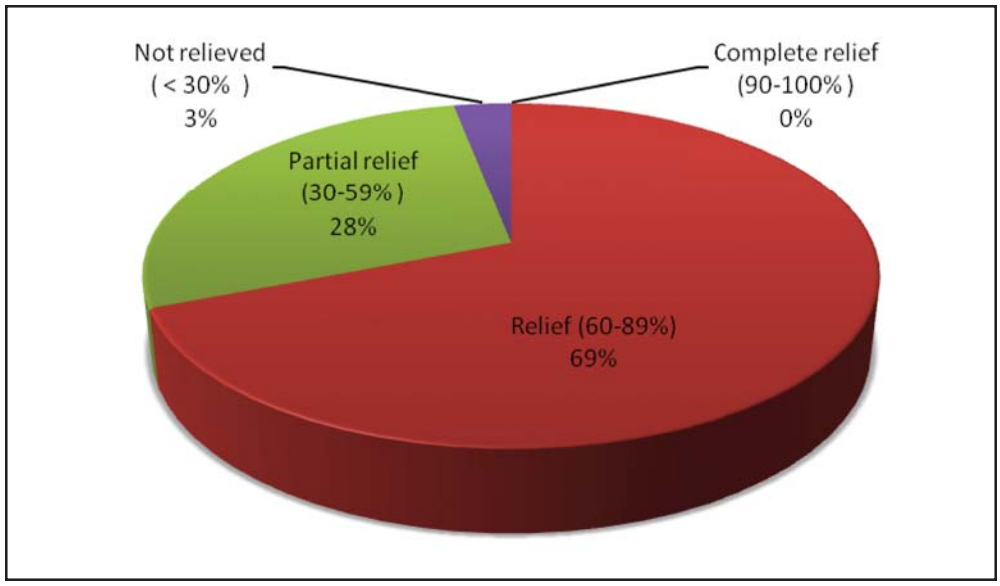
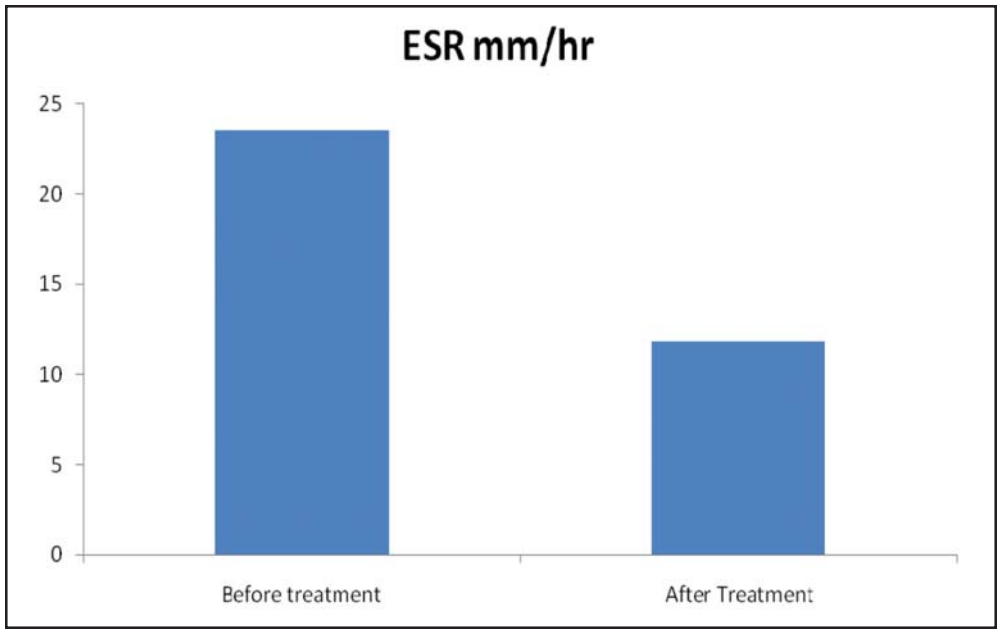


Figure 3: ESR mm/hr before and after treatment of Unani classical drugs



In the present study, the efficacy of Majoon-suranjan,Safoof- suranjan and Raughen- suranjan were evaluated over a period of 84 days on the basis of improvement in the subjective parameters. The improvement in joint pain, tenderness, morning stiffness, swelling, restriction of movement and muscular weakness was statistically significant and 59.15%, 70.00%, 68.42%, 62.50%, 72.41% and 41.67% respectively. Majoon suranjaan is reported as a antiarthritic property in Animal model (Singh *et al.*, 2011). Many single and compound unani drugs subjected to experimental and clinical studies have shown very promising results. For instance Suranjan Shireen (Colchicum autmnale) contain colchicine which is approved by USFDA for the treatment of Gout and familial medeterranean fever (Anonyms, 2014), Buzidan (Pyrethrum Indicum) was shown to produced significant analgesic and anti-inflammatory effect (Tajuddin, 1982). Maghz-e-Tukhme–e-Tarbooz *(Citrullus vulgaris*), Maghz-e-Tukhm-e-Badranjboya (Nepeta Hindostana) were shown to analgesic and antipyretic effects and compound formulations such as Safoof suranjan and Majoon suranjan (Ahmad,1997) have been reported to possess striking anti-arthritic activity and Raughen suranjan is a reputed and well-known drug in unani medicine and is used for locally application as anti-inflammatory and anti-arthritic agent. As main ingredients- Suranjan talkh (Colchicum luteum) and RoghanZaitoon (Olea Europea) were shown to anti-noceptive and anti-inflammatory effects (Nair, 2012; Fezai *et al.*, 2013)

Out of 29 cases, 18 cases were having RA factor positive and 24 cases had CRP positive and after the treatment of Unani drugs they had found negative. SGOT, SGPT, B. Urea and Serum creatinine were found in normal limit before and after treatment. There had no any change found in TLC, DLC, eosinophils, monocytes at baseline and after the treatment. Results suggest that the Unani classical drugs may be useful as potent drugs for the management of Waja-ul-Mafasil (RA). At the base line ESR increased, which was significantly reduced after treatment of Unani classical drug ($p<0.05$). Results are shown in the fig-3.

Conclusion

The classical Unani pharmacopoeial drugs, *MajoonSuranjan, SafoofSuranjan, RaughenSuranjan* in an unique combination of important Unani ingredients. Out of 29 cases, 20 (69%) were relief, 08 (28%) partially relief and 01 (3%) shows no response of drugs. It is also anti-inflammatory, antipyretic and analgesic actions reduced ESR, reduction of soft tissue and swelling, X-ray achieved and relief from clinical signs & symptoms. In view of the results achieved after studying 29 cases with the Unani Pharmacopoeial drugs. The study may be claimed as good result, safe remedy of arthritis. However, large controlled studies are required to reach at a final conclusion.

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