

Food Supplement for Therapy of HCV

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Abstract

Hepatitis C is a progressing global health problem. The expense of the exciting regimen for treatment is not available for many patients. Herbal medicines have been used as complementary therapy in the treatment of liver diseases for a long time. Fifty one patients with hepatitis C have been seen in our outpatient clinic, with twelve patients as control. Patients were interviewed to obtain detailed clinical data before and after treatment. The herbal medicines used in the treatment of HCV are Milk Thistle, Phyllanthus, Garlic, Cinnamon, Parsley, Black seed and AKHY-J-25 (mixture of herbs). Every patient received single oral capsule of herbal preparations powder, in early morning on an empty stomach with two cups of water and simple breakfast after two hours, from three months to two years, and twelve patients as control received placebo. The results showed 20% of patients had no detectable HCV RNA in serum at 24 week treatment, 72.6% showed clinical and biochemical improvement with decline of HCV RNA to lower limit and 7.4% showed clinical and biochemical improvement without change in level of HCV RNA.

Keywords: Hepatitis C; Herbal medicine; Liver; HCV RNA

Introduction

The Civilization in Ancient Egypt was not only the pyramids and tombs, but it involved all aspects of human life. Health and wellbeing was one of the most cared arts by the pharaohs. Most of the complementary medicine modalities were originated from ancient Egyptians. The Ancient Egyptians were quite advanced in their diagnosis and treatments of various illnesses [1].

Ebers papyrus, written about 3500 years points to the fact that ancient Egyptians applied plants such as mandrake for pain relief and garlic for the treatment of heart and circulatory disorders [2].

According to WHO [3] herbal medicine is plant derived material or preparations with therapeutic or other human health benefits, which contain either raw or processed ingredients from one or more plants. In some traditions, material of inorganic or animal origin may also be present.

The acute hepatitis C infection spread through transfusion of blood and blood products and transplantation of solid organs from infected donors, injecting drug use, unsafe therapeutic injections, occupational exposure to blood contaminated with needle sticks, birth to an infected mother, sex with an infected partner, and sex with multiple partners [4,5].

Chronic hepatitis C is associated with significant morbidity and mortality as a consequence of progression to cirrhosis, hepatocellular carcinoma, and liver failure. Current treatment for chronic hepatitis C with pegylated interferon (IFN) and ribavirin is associated with suboptimal responses and numerous adverse effects number of botanical products has been used to treat hepatic disorders [6].

Egyptian flora, the most diverse in the world, has become an interesting spot to prospect for new chemical leads or hits due to its species diversity. It has become clear that in Egypt many plants and herbs might provide effective antioxidant and anti cancer therapeutics [7].

WHO has approved the use of traditional medicines as a part of the health program for the treatment of various diseases. According to its estimate, the global demand for traditional medicine increased at an annual rate of 8% during the period 1994-2001, while in United States and Europe, it has grown at an average of 10% per year. According to

WHO survey 80% of populations living in the **developing countries** rely almost exclusively on traditional medicine for the primary health care needs [8,9].

It is a universally accepted fact that good health plays an important role in human development. WHO defines good health as a state of complete physical, mental, and social well-being and not merely an absence of disease or infirmity [10].

Flavonoids are present in most plants and concentrated in seeds, fruit skin or peel, bark, and flowers, which are having antibacterial, anti-inflammatory, antiallergic, antimutagenic, antiviral, antineoplastic, antithrombotic, and vasodilator actions. Flavonoids have been shown in a number of studies to be potent antioxidants, capable of scavenging hydroxyl radicals, superoxide anions, and lipid oxygen radicals due to lipid peroxidation [11].

The popular herbal supplement used in different centers all over the world as immuno-modulator and powerful antioxidants including, Milk Thistle which has therapeutic effect on hepatitis C virus lifecycle [12], Phyllanthus act as antioxidant [13], Garlic has anti-liver cancer [14], Cinnamon, has immuno-modulator [15], parsley, has Diuretic effect [16] and Black seed has anti-cancer [17].

Thus there are many patients who have no other Food and Drug Administration approved options to eliminate HCV and prevent progression of liver diseases. As a result, many individuals have opted for complementary and alternative medicine based approaches, including botanicals to treat their chronic hepatitis C, indeed, as many as 13% to 23% of American patients with chronic liver disease use botanical medicines, with silymarin being the most popular [18,19].

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Materials and Methods

Fifty one volunteer patients, 35 males with mean age 42 ± 6 and 16 females with mean age 42 ± 8 , with hepatitis C have been seen in our outpatient clinic, with twelve patients as control, 10 males with mean age 41 ± 8 and 2 females with mean age 32 ± 5 .

Each patient investigated to detect the presence of HCV RNA in serum by PCR. HCV RNA was purified and amplified in tubes coated with a solid-phase matrix that irreversibly bounds nucleic acid during the extraction step. After reverse transcription-PCR, the amplicon was adsorbed to the original extraction matrix for purification and use in the subsequent sequencing reactions [20].

In addition to other investigations which included the following: CBC (Hb, Platelet, WBCs, Neutrophil and Lymphocyte), liver function tests (SGPT, SGOT), Kidney function tests (Blood urea, Creatinine) and blood sugar before and after therapy, the exclusion criteria includes smoker, obesity, generalized debilitating diseases, hepatic failure, coexistent liver diseases, serious medical disorders, active alcohol abuse, and history of a severe psychiatric condition.

Every patient received single oral capsule 750 mg of well prepared mixed herbal powder, composed of traditional Egyptian herbal medicine in the form of Milk Thistle, Phyllanthus, Garlic, Cinnamon, Parsley, Black seed and AKHY-J-25 (mixture of herbs), early morning on an empty stomach with two cups of water and simple breakfast after two hours, from three months to two years and twelve patients as control received placebo.

The Milk Thistle has therapeutic effect on hepatitis C virus lifecycle [12], Phyllanthus act as antioxidant [13], Garlic anti-liver cancer [14], Cinnamon act as immune-modulator [15], Parsley has diuretic effect [16], Black seed act as anti-cancer [17] and AKHY-J-25 (mixture of herbs), containing more than 400 Flavenoids, in addition to protein, carbohydrate and fat.

Questionnaire was routine interview of patients and control which seen in the outpatient clinic by physician with declare of the patient for receiving herbal medicine voluntarily, with disappearance of the symptoms of the patients between 90% to 100%, after one month of therapy without any side effects of the drug (Questionnaire I).

Questionnaire I

Declare of patient for receiving herbal medicine voluntarily, with disappearance of symptoms of the patients between 90% to 100%, after one month of therapy, without any side effects of the drug.

Approval: Declaration by the patient or control

I (patient name) had agreed voluntarily with my will and I am in my powers of mentality, I take the herbal medicine, which designed composition botanical mixed of several plants, and put it in capsules, under supervision of Dr. Abdel khalek H. Younes. I received treatment free of charge on the extension of treatment periods, which dealt with the supplement.

After finishing, the patient from the treatment period, which ranged between three months and two years, with the disappearance of the symptoms that patient was complained and the complain rate after one month of therapy ranging between 90% to 100% without any side effects of the drug. Patients were also asked the symptoms associated with HCV with declare of the patient for receiving herbal medicine voluntarily; with enumerate the disappearance of symptoms without any side effects of drug (Questionnaire II).

Questionnaire II

Declare of patient for receiving herbal medicine voluntarily, with enumerate disappearance of symptoms without any side effects of drug.

Adoption: I (The name of patient or control)

I (patient name) have deal with complementary herbal medicine, under supervision of Dr. Abdel khalek H. Younes, as dietary supplement to help me to overcome the HCV. During the treatment period, I was having one capsule per day, on an empty stomach. All symptoms disappear after one month of therapy, and at same time I did not suffer or complain of any side effects of treatment over the treatment period of 3 month to two years. Do you get rid of the the following symptoms?

- 1 - Generalized weakness Yes/No
- 2 - Loss of appetite Yes/No
- 3 - Nausea and vomiting Yes/No
- 4 - Dyspepsia and distention Yes/No
- 5 - Fatigue and weakness Yes/No
- 6 - Increase the feeling drowsy Yes/No
- 7 - Poor memory, and concentration Yes/No
- 8 - Mood disorder Yes/No
- 9 - Pain in the abdomen Yes/No
- 10 - Yellow color of eyes and skin Yes/No
- 11 - Joint and muscle pain Yes/No
- 12 - Erectile dysfunction Yes/No
- 13 - Anxiety, insomnia and depression Yes/No

Statistical significance was demonstrated by using the Student's *t* test. Statistical analysis was performed using SPSS software version 66.

Results

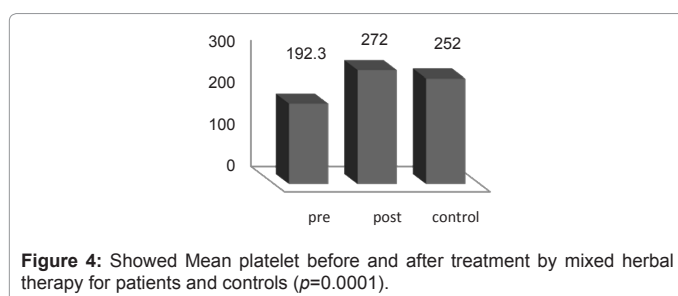
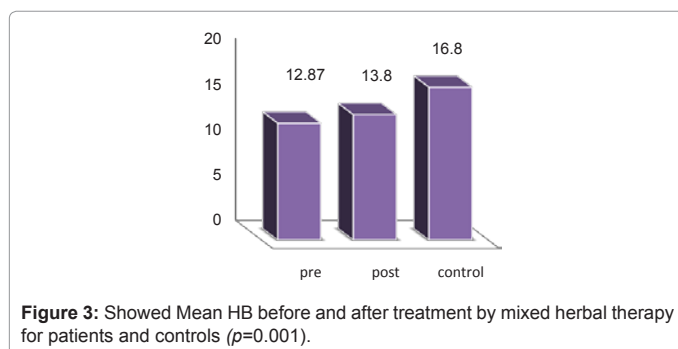
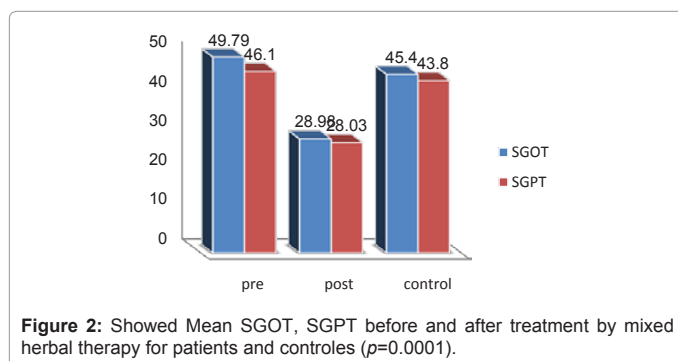
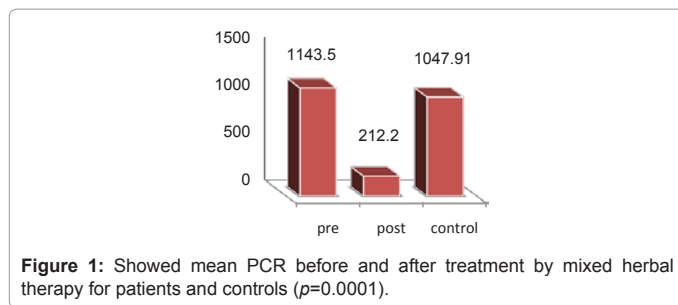
Fifty one volunteer patients with hepatitis C have been seen in our outpatient clinic with twelve volunteer patient's control, patients were interviewed to obtain history and detailed clinical data before and after treatment.

All the patients received the herbal medicine powder in the form of capsules and volunteer control patients received placebo, with follow up of the patients and control for three months to two years.

The powder of each capsule containing 750 mg of herbal medicine and composed of Milk Thistle, Phyllanthus, Garlic, Cinnamon, parsley, Black seed and AKHY-J-25 (mixture of herbs).

The results showed that 20% of patients had no detectable HCV RNA in serum at 24 week treatment. 72.6% showed clinical and biochemical improvement with decline of HCV RNA to lower limit and 7.4% showed clinical and biochemical improvement without change in level of HCV RNA.

Mean HCV RNA (Figure 1), SGOT, SGPT (Figure 2), platelets (Figure 4), WBCs (Figure 5), neutrophils (Figure 6). Lymphocytes (Figure 7) showed very highly significant results ($p=0.0001$), HB (Figure 3), showed highly significant improvement ($p=0.001$), Creatinine



showed significant improvement ($p=0.009$), and blood urea and RBS showed non-significant changes ($p=23.98$, $p=2.2$) respectively in spite of improvement of blood urea and RBS to normal level in comparing of its result before and after treatment (Table 1).

Discussion

Herbs played a major part in Ancient Egyptian medicine. The plant medicines mentioned in the Ebers Papyrus, and temple of the bulls at Saqqara includes Cinnamon, parsley, Garlic [21], black seed have been found in several sites from ancient Egypt, including Tutankhamen's tomb [22] and milk thistle [23], in addition to Phyllanthus [24].

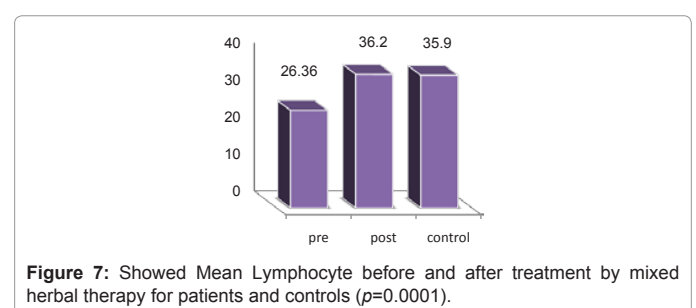
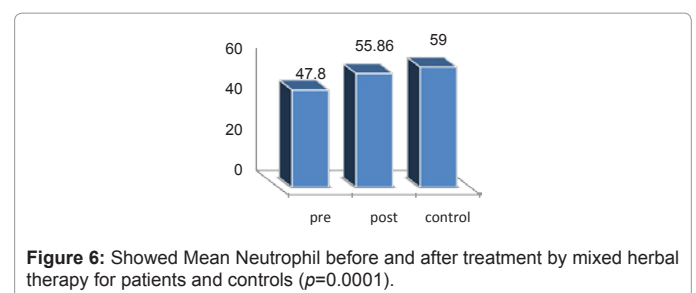
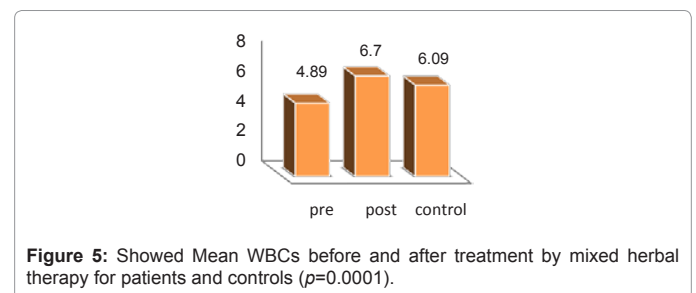
The herbal medicine as natural plant, are not only the main source of nutrients, but they are also rich in phytochemicals which acts as immune-modulation, antivirus, antioxidant anti-cancer, anti-inflammatory effects and improved general health of human being [25,26,27].

Perceived benefits from herbal medicine therapy include more energy and reduction in fatigue, as well as positive effects on the immune system [28].

Balanced diet, including protein, carbohydrate, fat, minerals and vitamins play an important role for improvement of immune system of human being and protection health of an individual and at the same time protect himself against different types of diseases included HCV [29,30].

HCV is a major cause of liver disease. There are about 175 million HCV patients worldwide that constitute 3% of world's population. The main route of HCV transmission is parental; however 90% intravenous drug users are at highest risk [31]. It is associated with cirrhosis, hepatocellular carcinoma, and liver failure. HCV with pegylated interferon (IFN) and ribavirin is associated with suboptimal responses and numerous adverse effects [6]. So HCV is necessitating, effective, inexpensive, and less toxic treatments. Antioxidant therapy has a mild beneficial effect chronic HCV infection patient who is non-responders to interferon. Combined antiviral and antioxidant therapy may be beneficial for these patients [32,33].

Giese [34] showed 43% of patients who used complementary and



Variables	PRE	POST	Control	P1	P2	P3
HCV RNA 10 ³ /ml	1143.5 ± 30.02	212.2 ± 73.3	1047.91 ± 80.2	0.047*	0.0001*	0.0001*
SGOT IU/ML	46.1 ± 5.29	28.03 ± 2.49	43.8 ± 3.9	0.82	0.0001*	0.0001*
SGPT IU/ML	49.79 ± 6.18	28.98 ± 2.74	45.4 ± 2.2	0.83	0.0001*	0.0001*
HB %/gm/dL	12.87 ± 0.169	13.8 ± 0.18	16.8 ± 0.33	0.001*	0.001*	0.001*
Platelets 10 ³ /cm	192.3 ± 7.27	272 ± 14.06	252.2 ± 9.13	0.001*	0.188	0.0001*
WBCs/cm	4.89 ± 0.17	6.7 ± 0.26	6.09 ± 0.41	0.0001*	0.341	0.0001*
Lymphocyte %	26.36 ± 1.39	36.2 ± 1.49	35.9 ± 2.01	0.0001*	0.555	0.0001*
Neutrophil %	47.8 ± 2.08	55.86 ± 1.23	59.0 ± 1.34	0.0001*	0.752	0.0001*
Urea mg/dl	30.1 ± 1.3	28.6 ± 1.15	33.6 ± 1.9	0.025	0.056	23.98
Creatinine mg/dl	2.01 ± 0.75	1.49 ± 0.6	1.07 ± 0.65	0.01*	0.0001*	0.009*
Blood sugar mg/dl	96.04 ± 3.3	100.98 ± 3.04	103.1 ± 2.1	1.94	2.52	2.2

PRE: Pre-therapy; POST: Post-therapy from three months to two years; P1: Compare between PRE and control; P2: Compare between POST and control; P3: Compare between Pre and Post

Table 1: HCV RNA, Liver Function, CBC, Kidney Function and Blood Sugar for Patients and Controls.

alternative medicines (CAM) used it for liver disease. Another study [35] detected that specifically surveyed clinic patients, found that 37% of patients that had used or were using CAM, 20% were using the CAM therapy for chronic hepatitis and 17% were using it for other reasons. The use of CAM for liver disease may actually be higher outside western populations; a study by Yang et al. [36] looking at CAM use in Taiwanese patients found as many as 66% of patients used CAM.

This mean that the popularity of herbal medicine which become effective, inexpensive, and less toxic, becomes now a days as facts for control and treatment of many dangerous diseases of human being, included HCV due to its antioxidant effect [37].

Silymarin, extracted from the milk thistle used widely among 10 study centers. No beneficial effect of silymarin was found on serum alanine aminotransferase or HCV RNA levels. While Seff et al. [19] reported benefits of herbal medicine uses included reduction in fatigue, boost in the immune system and improved gastrointestinal function. No adverse effects of herbal medicine use were reported including milk thistle [38]. Polyak et al. [39] milk thistle extract, inhibits hepatitis C virus infection and also acts as antioxidant, anti-inflammatory, immunomodulator, actions and contribute to hepatoprotective effects.

The mechanisms of silymarin's antiviral action appear to include blocking of virus entry and transmission, possibly by targeting the host cell [12]. Silymarin also use among patients with advanced hepatitis C-related liver disease is associated with reduced progression from fibrosis to cirrhosis, but has no impact on clinical outcomes [40].

United States multicenter Phase II trial to evaluate silymarin for treatment of patients with chronic hepatitis C infection who had failed to respond successfully to previous IFN-based therapy are common and must be addressed to conduct rigorous trials of botanical products [5].

Clinical studies which discussed before, of using of only one herbal medicine for treatment of HCV like Milk Thistle is not enough to overcome the degenerative effects of HCV disease and capability of get rid of hepatitis c virus, because only one herbal medicine is not enough to prevent attacks of liver cells by virus, clear the liver from virus and repair its cells after chronic inflammation, cirrhosis and fibrosis. So it is necessary to use mixtures of herbal therapy to increase its synergetic effects against HCV and decrease of its side effects.

In this current study, 51 Patients, 35 males and 16 females, with hepatitis C have been seen in our outpatient clinic, with 12 patients as control, 10 males and 2 females. All patients received mixed herbal medicine powder in the form capsules and the patients control received

placebo, Following up of the patients and control for three months to two years. Results showed that twenty percent of patients had no detectable HCV RNA in serum at 24 week treatment, 72.6% showed clinical and biochemical improvement with decline of HCV RNA to lower limit and 7.4% showed clinical and biochemical improvement without change in level of HCV RNA.

This mean that the used of mixture herbal medicine Milk Thistle, Phyllanthus, Garlic, Cinnamon, parsley, Black seed and AKHY-J-25 (mixture of herbs), has therapeutic effect on hepatitis C virus lifecycle [12], antioxidant [13], anti-liver cancer [14], immunomodulator [15], Diuretic effect [16], anti-cancer [17], and it contains more than 400 Flavenoids, respectively which are proficient in inhibiting the HCV replication rate and its side effects with no side effect of drugs for 3 months to 2 years.

However the mechanism of action of this medicine is not fully understand. Thyagarajan et al. [41], proved that Milk Thistle act as anti-oxidative, antilipidperoxidative, antifibrotic, anti-inflammatory, immunomodulating and liver regenerative. Extensive studies on Phyllanthus A confirmed that this plant being anti-viral against HBV and HVC, hepatoprotective and immunomodulator, and anti-inflammatory properties.

Significant therapeutic results of using of traditional Egyptian herbal medicine, in this study is due to its synergistic effects with prescience of balanced diet in each single capsule, contains sufficient amounts of fiber and the various nutrients in the form of proteins, carbohydrates, fats, vitamins, minerals, flavenoides and water for the proper maintenance of good health with boost and support the immune system. As Guimarães et al. [42], reported that the most potent antioxidant activity was found in combinations of different herbs, suggesting synergistic effects. The presences of different types of flavenoides, essential amino and fatty acid, Enzymes & Co-enzymes and other phytochemicals which act as anti-oxidative, antifibrotic, anti-inflammatory, immunomodulating and anti-viral effects. So the synergistic effect of using mixture of herbs are designed to work together to produce a gentle, balanced and greater effect to correct underlying imbalances than temporary relief [24,25,26].

Immune system plays a crucial role in suppressing and eliminating virus. In HCV patient successfully used alternative medicines to improve general health of patients, decrease viral loads, decrease liver enzyme levels or even eliminate the virus completely, with no side effect. Therefore it is a very consistent trend in treatment of HCV is to concentrate tremendous emphasis on improving the immune system [14].

In this study the general condition of the patients improved and all symptoms disappear completely after one month of starting therapy, with no side effect along the time of therapy, from 3 months to 2 years. This current study agreed with criteria described by WHO [3] that traditional Medicine Strategy was developed, with four primary objectives; enhancing safety, efficacy and quality; ensuring access; and promoting rational use.

Side effect of the using of mixed herbal medicine in this study was zero due to its safety and lower minimal dose of mixture of each herbs. This current study agreed with criteria described by Ernst [43], the safety and efficacy, as well as the quality control, of traditional medicine and CAM have become important concerns for both health authorities and the public.

In this study also, there is no anemia for patient used the mixed of herbal medicine but the hemoglobin levels showed highly significant improvement ($p=0.001$), after using the herbal therapy more than before and at the same time anxiety, stress and sleep disturbance, depression and health related quality of life in those patient with HCV improved, and this increase the efficacy of herbal therapy [44,45].

Also in this current study the platelets count, WBCs, neutrophil, and lymphocyte showed very highly increased significant results ($p=0.0001$) indicated that haemostatic and immune systems regulate each other with good immunity helping for production of endogenous cytokines including interferon with repair of liver cells, prevent fibrosis, cirrhosis and scar of liver and contribute to spontaneous resolution of HCV virus [46,47].

In view of the above mentioned study Creatinine showed significant improvement ($p=0.009$), and Blood urea and RBS showed non-significant changes ($p=23.98$, $p=2.2$) respectively. In spite of that there was improvement of blood urea and RBS to normal level, in comparing of its result before and after treatment. Herbal medicine has antioxidant properties proved their significant effects not only in preventing but also curing diabetes and various kidney diseases [48].

Various clinical trials have been shown that in order to increase efficacy and rate of absorption of herbal medicine, to become more effective and more protection for the liver cells. Phytosomes are advanced forms of herbal products that are better absorbed, utilized, and as a result produce better drug delivery than conventional herbal extracts [49].

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