

ORIGINAL ARTICLE

Therapeutic effects of diet and ginger supplementation at different doses on serum C-reactive protein and Erythrocyte Sedimentation Rate of hospitalized arthritic patients: A Randomized Cross-Over Study

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ABSTRACT

Ginger is a culinary herb, widely used in South Asia as traditional and nutraceutical zesty spice. Clinical trials suggest that ginger modulates biochemical pathways activated in chronic inflammation. Ginger has been proven as a therapeutic spice in many medical conditions including inflammation, arthritis and many infections. Current clinical trial was designed to evaluate the therapeutic potentials of encapsulated ginger and diet based on gingerol serum CRP and ESR level in arthritic patients. For clinical trial 24 female patients aged ≥ 30 years were randomly selected from the DHQ Hospital Jhelum. They were divided into six groups, each of four patients. A Performa was designed to collect data of patients including their anthropometric, biochemical, clinical, dietary and general health status assessment. During 30 days of trial, decrease in serum CRP level in six groups D0, D1, D2, D3, D4 and D5 was 58.76 ± 0.23 , 54.25 ± 0.29 , 50.25 ± 0.28 , 46.25 ± 0.28 , 42.11 ± 0.31 , 37.59 ± 0.35 respectively. Mean ESR values (table) for D0, D1, D2, D3, D4, D5 were 48.50 ± 0.22 , 43.24 ± 0.28 , 39.25 ± 0.28 , 35.25 ± 0.28 , 31.25 ± 0.28 , 27.25 ± 0.28 $\mu\text{g/L}$ respectively. Results showed that compared to control the diet based on ginger and encapsulated ginger have clinical healthy effects on arthritic patients.

Keywords: Nutraceuticals, anthropometric, biochemical, encapsulated ginger, serum CRP level.

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INTRODUCTION

Arthritis is an inflammatory disease of joints which is prone to various underlying physiological malfunctioning and etiologies while Rheumatoid arthritis (RA) is defined as chronic inflammatory disease of our immune system, complicated with obdurate aches and disabilities [1]

RA influences 0.5-1 % of overall world population. In the urban population of southern Pakistan, Karachi the prevalence of RA is reported to be 0.142% whereas; in northern Pakistan the estimated prevalence is 0.55% [2]

The healthy human body is equipped with a powerful set of tools for resisting the attack of invading microorganisms (such as viruses, bacteria, parasites). Unfortunately, this set of tools known as the immune system, sometimes goes awry and attacks the body itself. In some cases; however the cells of our immune system get out of control. They turn against the body itself and begin to destroy healthy tissues. This results in auto immune disease. Autoimmune diseases affect about five percent of people living in industrialized nations; over 80 of these "auto aggressive" diseases are now recognized [3]

In this disease, the muscle of strength is compromised along with abrupt loss of muscle function is ensured by inflammation and swelling at the site of prevailing disease. This may aggravate a rash and an intensifying a pain response at the affected site which may lead towards the failure of joint function. The extent of damage is dependent to the intensity as well as the length of an inflammation. Failure of joint

function outcome is the deformity, unable to move and in severe cases handicap. Epidemiology confers to almost 12,000 people in UK suffer from RA per annum and as a whole, the incident of RA in women prevail 2-4 times more than in men. Whereas according to recent survey, the prevalence of RA for both female and male occur at the age of 40-70 years, however people of all ages can be effected by RA[4]

At the cellular level, histological studies have revealed important differences between synovial tissue in RA and PsA[5]. Angiogenesis is deregulated in both conditions and abnormal vessel morphology and function has been reported. Increased straight, branching vascularization is a prominent feature observed in RA joints, whereas the formation of elongated, bushy, torturous blood vessels is a more marked feature of the PsA joint[6]. In the RA joint there is increased macrophage infiltration and subsequent synovial invasion compared with that observed in PsA. As a result, lining layer hyperplasia observed in RA is more striking than that observed in PsA. Conversely, PsA is characterized by more extensive infiltration of polymorph nuclear cells. The extent of T-cell and B-cell infiltrations comparable in both conditions and the formation of germinal centers (zones of T-cell and B-cell proliferation) is observed in both PsA and RA joints[7].

RA affects different people in different ways. Symptoms may slowly develop over several years, or the disease may progress quickly. Symptoms may be mild or very severe. You may go through phases called "flares" or "flare-ups" when symptoms are severe. At other times, it may seem as if the disease and its symptoms have gone away. This is called "remission." Joint pain and swelling may happen slowly and may occur over weeks or months. The small joints in the wrists and hands are often inflamed first. Over time, other joints may be painful and swollen due to RA[8].

Signs and symptoms of RA include painful joints, swollen joints, stiffness in joints, particularly in the morning, low fever, fatigue, loss of appetite, feeling weak, lumps under the skin, especially on the hands or elbows, weight loss, over time, decreased range of motion, dry eyes and mouth[9].

Food and nutrients are the pillars of contemporary nutrition, due to the anesthetizing impact of profit-oriented market, diet and medicine have taken the divergent pathways. Nowadays, the role of diet and nutrition is gradually becoming an important public health concern throughout the world[10]. Food remains a feasible and logical approach to impact favorable condition for normal body functioning. The use of natural product as medicine has gained immense popularity and have a high functional and nutritional evidence [11].

Neutraceutical and functional foods provide an opportunity to promote health quality by assisting the means to reduce the oncogenic events. Phyto-nutrients of plant origin are the most prominent part of neutraceutical based diets. Nutrition articulates about the basic nutritional requirements for general health while pharmaceuticals explains the remedial approach against sickness. The convergence of both these ideas give rise to the modern stating of neutraceutical encompassing both health as well as therapeutic effect [12][13]. These are safe and economically sound due to their numerous health endorsing properties.

MATERIAL AND METHODS

Procurement of raw material

Ginger was procured from local market of Faisalabad

Sample preparation

Ginger was cut into small pieces after peeling in order to obtain desired size. Afterwards, slices were oven dried and ground to fine powder using grinder.

Encapsulation of ginger

Ginger powder was weighed and packed into capsules. Encapsulation is done by following the method of Gonlachanvit *et al* [17]. Store finished capsules in glass jars away from heat and moisture

Participants and screening procedure

The study was carried at DHQ Hospital Jhelum. For this study, 24 patients of Rheumatoid arthritis were selected. They were divided into six groups, each of 04 patients. All the selected patients were enrolled through direct personal communication. Subjects were selected based on meeting the following inclusion criteria: free from other chronic diseases, aged 30 years or above and those who signed written consents. Subjects were excluded from the study for any of the following reasons: Dislike for ginger, unwillingness to give blood via finger prick, smoking restricted dietary habit, unusual weight alternation > 10 pounds in the last 3 months, take medications regularly and not willing to participate in the study.

Diet and Ginger dosage

Groups N=06	Experimental design N=06
Control 1	Normal diet
G1	Normal diet + 150 mg of ginger capsule
G2	Normal diet + 300 mg of ginger capsule
Control 2	Diet plan
G3	Diet plan + 150 mg of ginger capsule
G4	Diet plan + 300 mg of ginger capsule

Data collection tool

Standardized Questionnaire and expert observations were used for collection of different types of data given below.

Anthropometric measurements

The anthropometric measurements including height by standio-meter, weight by digital weight scale, BMI, IBW and waist circumference measurements by inelastic measuring tape were noted for each patient according to standard method.

Blood sample collection

Three cubic centimeter (CC) blood was taken by phlebotomist from the peripheral vein of the each patient with the help of disposable syringe. Blood was immediately transferred into dry clean and screw capes test viles. These viles contain clotting gel which coagulate blood sample. After the formation of complete clot, samples were centrifuged with the help of centrifuged machine at 5000 revolution per minute (rpm). Serum was removed and collected in RNA free serum cups and stored in freezer at 20°C, till analyzed.

Biochemical tests

Blood parameters include; C- reactive protein and erythrocyte sedimentation rate were analyzed by kit method[16].

Determination of C- reactive protein

Serum CRP concentration was determined by Immuno-turbidimetric test by the principle of photometric measurement of the antigen-antibody reaction of antibody to human CRP with CRP present in the sample.

Determination of erythrocyte sedimentation rate

1.2 mL of the venous blood was collected and opened the citrate tube. Filled the tube with blood up to the level of 1.25 mL then closed the tube firmly and was mixed. . Westergren tube was introduced into opened citrate tube. The blood meniscus must reach "0 mm" level .Westergren tube was placed into the vertical stand (for an hour) or into the inclined (oblique) stand (for 7 and 10 minutes) and then recorded the number of mm to which erythrocytes have settled.

Clinical signs and symptoms

These signs and symptoms include shortness of breath, hypertension, stomach burning, constipation, pain and swelling around the joint, making it tender and warm, stiffness in the morning, tiredness and rheumatoid nodules were noted on daily basis.

Dietary intake assessment

Dietary intake was assessed by 24 hr recall method to evaluate dietary intake. Dietary intake included Energy intake and kcal (RDA). The intake of nutrients was worked out on the basis of estimated quantities of various foods taken by the RA patients using food composition table developed for patients. Macro nutrients like protein, carbohydrates and fat were calculated by using food composition tables taking into account the quality of caloric food intake by hospitalized patients.

Caloric Recommended Dietary Allowance (RDA)

Caloric RDA of each individual was calculated to guide them how much calories they should take. It was calculated by multiplying BMR with their activity level of 1.3 for Sedentary, 1.5 for moderately active and 1.7 for active patients.

Calculations and Statistical analysis

SPSS version 16 was used for analyzing statistical data for examining the effect of treatment, effect of time and effect of time by treatment interaction.

RESULTS**Demographic and Anthropometric characteristics of studied patients**

The demographic and anthropometric characteristics of the studied subjects are shown. Their mean age, weight, height waist circumference, BMI for female patients were 41.4 ± 0.72 , 58.8 ± 5.75 , 151.2 ± 2.8 ,

74.2 ± 6.78, 21.5 ± 3.9 respectively. For male patients the mean age was 47.9 ± 0.84, weight was 67.5 ± 8.15, height was 164.72 ± 7.4, waist circumference was 81.46 ± 11.4, and BMI was 24.22 ± 3.7

Table 1 Demographic and anthropometric characteristics of studied subjects (n = 24)

Variable	Mean ± SD	
	Female	Male
M/F	08	16
Age(y)	41.4 ± 0.7	47.9 ± 0.84
Weight (kg)	58.8 ± 5.7	67.5 ± 8.15
Height (cm)	151.2 ± 2.1	164.72 ± 7.4
Waist circumference (cm)	74.2 ± 6.7	81.46 ± 11.4
BMI(kg/m ²)	21.5 ± 3.9	24.22 ± 3.7

BMI: Body mass index, SD= Standard deviation M= Male, F=Female

Serum CRP level

Mean squares for serum CRP level (Table 4.5.1) showed a significant difference ($p < 0.01$) in C- reactive protein level due to the difference in dietary pattern of groups and the days. Results were also found non-significant with respect to interaction of treatment and interval for groups.

The effect of diet and the feeding periods (days) on the values of CRP levels are presented in Table. During 30 days of trial, decrease in serum CRP level in six groups D0, D1, D2, D3, D4 and D5 was 58.76±0.23, 54.25±0.29, 50.25±0.28, 46.25±0.28, 42.11±0.31, 37.59±0.35 respectively. Reduction in serum CRP level recorded in group 5 which was treated with 300 mg of ginger powder along with the diet plan from 0 to 30 days was highly significant, because it contains healthy bioactive ingredients such as [6]-gingerol and shogol.

Table 2: Analysis of variance table for CRP.

Source of variation	Degrees of freedom	Sum of squares	Mean squares	F-value
Days	6	111.66	18.61	8.97**
Diet	5	8562.10	1712.42	825.06**
Days x Diet	30	14.73	0.49	0.24NS
Error	126	261.51	2.08	
Total	167	8950.01		

NS = Non-significant ($P > 0.05$); * = Significant ($P < 0.05$); ** = highly significant ($P < 0.01$)

Table 3: Days x Diet Mean ± SE for CRP

Days	Diet						Mean
	D0	D1	D2	D3	D4	D5	
0	59.50±0.65	55.50±0.65	51.50±0.65	47.50±0.65	42.75±1.11	38.50±0.65	49.21±1.52a
5	59.00±0.65	55.00±0.96	51.00±0.65	47.00±0.65	43.00±0.65	38.38±1.01	48.90±1.48a
10	58.75±0.65	54.75±0.65	50.75±0.65	46.75±0.65	42.75±0.65	38.25±0.91	48.67±1.47ab
15	58.50±0.65	54.50±0.65	50.50±0.65	46.50±0.65	42.50±0.65	38.00±0.91	48.42±1.47ab
20	58.50±0.65	54.00±0.65	50.00±0.65	46.00±0.65	42.00±0.65	37.50±0.91	48.00±1.50ab
25	58.56±0.70	53.50±0.65	49.50±0.65	45.50±0.65	41.50±0.65	37.00±0.91	47.59±1.53bc
30	58.50±0.65	52.50±0.65	48.50±0.65	44.50±0.65	40.25±0.85	35.50±0.87	46.63±1.61c
Mean	58.76±0.23a	54.25±0.29b	50.25±0.28c	46.25±0.28d	42.11±0.31e	37.59±0.35f	

Means sharing similar letter in a row or in a column are statistically non-significant ($P > 0.05$). Small letters represent comparison among interaction means and capital letters are used for overall mean.

Serum erythrocyte sedimentation rate (ESR)

Mean squares concerning ESR (Table 4) revealed that diet presented significant differences on ESR in all studies and whilst non-significant impact was observed for interaction. Mean ESR values (table-4) for D0, D1, D2, D3, D4, and D5 were 48.50±0.22, 43.24±0.28, 39.25±0.28, 35.25±0.28, 31.25±0.28, 27.25±0.28 µg/L respectively. It was noted that diets containing ginger powder efficiently decreased ESR level other than control group. Similarly, maximum decrease in ESR level was noted for D5 (diet plan + 300mg ginger powder) that reduced significantly from 28.50±0.65 to 25.50±0.65 µg/L as a function of study intervals.

Table 4: Analysis of variance table for ESR.

Source of variation	Degrees of freedom	Sum of squares	Mean squares	F-value
Days	6	111.66	18.61	8.97**
Diet	5	8562.10	1712.42	825.06**
Days x Diet	30	14.73	0.49	0.24 ^{NS}
Error	126	261.51	2.08	
Total	167	8950.01		

NS = Non-significant (P>0.05); * = Significant (P<0.05); ** = highly significant (P<0.01)

Table 5: Days x Diet mean± SE for ESR.

Days	Diet						Mean
	D0	D1	D2	D3	D4	D5	
0	48.50±0.65	44.50±0.65	40.50±0.65	36.50±0.65	32.50±0.65	28.50±0.65	38.50±1.44 ^a
5	48.50±0.65	44.00±0.65	40.00±0.65	36.00±0.65	32.00±0.65	28.00±0.65	38.08±1.47 ^{ab}
10	48.50±0.65	43.75±0.65	39.75±0.65	35.75±0.65	31.75±0.65	27.75±0.65	37.87±1.48 ^{abc}
15	48.50±0.65	43.50±0.65	39.50±0.65	35.50±0.65	31.50±0.65	27.50±0.65	37.67±1.49 ^{abc}
20	48.50±0.65	43.00±0.65	39.00±0.65	35.00±0.65	31.00±0.65	27.00±0.65	37.25±1.52 ^{bc}
25	48.50±0.65	42.50±0.65	38.50±0.65	34.50±0.65	30.50±0.65	26.50±0.65	36.83±1.55 ^{cd}
30	48.50±0.65	41.50±0.65	37.50±0.65	33.50±0.65	29.50±0.65	25.50±0.65	36.00±1.60 ^d
Mean	48.50±0.22 ^a	43.25±0.28 ^b	39.25±0.28 ^c	35.25±0.28 ^d	31.25±0.28 ^e	27.25±0.28 ^f	

Means sharing similar letter in a row or in a column are statistically non-significant (P>0.05)

Small letters represent comparison among interaction means and capital letters are used for overall mean.

DISCUSSION

The current clinical trial was to explore and endorse the nutritional as well as nutraceutical profile of ginger powder by making ginger supplemented capsules. Nutraceutical potential was studied in contrast to rheumatoid arthritis, it was supposed that this is very helpful in contradiction of such diseases. Current findings are similar with the previous research work of Rong *et al.* [19] checked the safety assessment of ginger in human patients by observing their hematological metabolisms. They concluded that the CRP decreased non significantly from 71.44±23.7 to 66.8±20.2 with the passage of time and this surge was also observed in the CRP level of subjects of rheumatoid arthritis were fed on diet having ginger (250mg/kg body weight) in their diet as their CRP changed from 58.16±13.16 to 50.40± 9.50. With the high amount of ginger the CRP level further decreased.

The current findings are in agreement with the results of Bhandari *et al.* [20] used ginger powder (200mg/kg) based diet in arthritic patients to judge reduction in the ESR level during 20 days study trail. They noticed ESR level of normal humans' 50.1±6.0 µg/L and maximum level 200.09± 29.6 in arthritic group of patients. After the rheumatoid arthritis they used ginger powder in addition to their diet and established that the blood ESR level was lessened to 152.9±41.3 µg/L.

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AUTHOR CONTRIBUTIONS

FA designed and conducted the study.SK drafted the article. SL, US, SK critically revised the article. All authors read and approved the final version of the article. The authors declare that there are no conflicts of interest.

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