Arch Cardiovasc Imaging. 2016 February; 4(1):e38087. doi: 10.5812/acvi.38087.

Published online 2016 May 28. **Research Article**

The Effects of Curcumin on Left Ventricular Function in Patients with Chronic Renal Failure

Arezoo Khosravi,[1] Hesam Hashemi,[1] Maryam Moshkani Farahani,[1,*] Mitra Dolatkhah,[1] Zohreh Rostami,[2] and Younes Panahi[3]

[1]Atherosclerosis Research Center, Baqiyatallah University of Medical Sciences, Tehran, IR Iran
[2]Nephrology, Urology Research Center, Baqiyatallah University of Medical Sciences, Tehran, IR Iran
[3]Research Center for Chemical Injuries, Baqiyatallah University of Medical Sciences, Tehran, IR Iran

[*]*Corresponding author*: Maryam Moshkani Farahani, Atherosclerosis Research Center, Baqiyatallah University of Medical Sciences, Tehran, IR Iran. E-mail: moshkani_farahani@yahoo.com

Received 2016 March 29; **Revised** 2016 April 09; **Accepted** 2016 May 14.

Abstract

Background: Curcumin, a yellow substance found in turmeric, has not only antioxidative features and beneficial effects in the treatment of cancer, liver, heart, and pulmonary diseases but also anti-inflammatory and anticoagulative effects. This chemical has cardioprotective effects too.
Objectives: In this study, we examined the effects of curcumin on left ventricular (LV) function in patients receiving dialysis for chronic renal failure.
Methods: This study is a double-blind, placebo-controlled trial conducted on 35 patients with chronic renal failure undergoing dialysis in the dialysis center of Baqiyatallah hospital. The patients were randomly divided into 2 groups: the curcumin group (n = 20) and the control group (n = 15). The curcumin group received curcumin capsules at a dose of 500 mg every 8 hours for 6 weeks (1500 mg/d) and the control group received a placebo for 6 weeks at the same dose. Echocardiography was done before the use of the drug and once after the 6th week. Also, the ejection fraction (EF), representing LV function and size, was measured in both groups.
Results: The mean age was 44.2 ± 13.4 years for the curcumin group and 45.4 ± 6.2 years for the placebo group. The study population comprised 22 male and 13 female patients. There were no significant differences regarding demographic variables such as age, sex, and body mass index between the 2 groups. In the curcumin group, LVEF based on the volume changed from 50.6% ± 7.1% to 51.5% ± 6.8% (P = 0.130). In the curcumin group, LVEF based on the diameter changed from 51.8% ± 3.8% to 52.4% ± 3.5% (P = 0.112). The changes in the mean EF before and after the intervention were not significant in each group. The EF, based on ventricular volume and diameter, was not significantly different between the 2 groups. In addition, the pulmonary artery pressure mean in both groups did not significantly change after the intervention (P > 0.05).
Conclusions: The administration of curcumin in patients undergoing dialysis had no positive effects on enhancing LVEF and LV function. Further research is required to shed sufficient light on this issue.

Keywords: Curcumin, Left Ventricular Ejection Fraction, End-Stage Renal Disease, Dialysis

1. Background

The complications and abnormalities of the left ventricle (LV) are some of the most common problems among dialysis patients (1). For instance, in more than 72% of dialysis patients with chronic renal failure, LV hypertrophy is diagnosed (2). Heart problems in dialysis patients may impose significant additional costs and increase the probability of hospitalization and as such constitute the most probable cause of death among such patients (3).

Curcumin is a natural and yellow-colored material extracted from Curcuma longa (turmeric) with hepatic metabolism and intestinal excretion (4). Curcumin has anti-inflammatory effects by reducing the expression of inflammatory factors (e.g., NF-kB), enzymes (e.g., cyclohexane oxygenase-2 and 5-lipoxygenase), and cytokines such as TNF, IL-1, and IL-6 (5). Different studies on rats have reported the heart-related positive effects of curcumin in terms of the prevention of cardiac hypertrophy, cardiac muscle repair, improvement of cardiac function and reperfusion post myocardial infarction and ischemia (6-13). In different human studies, the positive effects of curcumin aside from those vis-à-vis cardiac disease have been reported on colorectal neoplasia (14), ulcerative colitis (15), diabetes type (2, 16) and obesity (17). One study reported that highly absorptive curcumin was able to improve LV di-

astolic function in hypertensive patients (18).

Although the positive role of curcumin in improving heart function in laboratory models has been proven 6, there is a dearth of relevant data on human models.

2. Objectives

Given the obvious benefits of reducing cardiac complications in patients with chronic renal failure undergoing dialysis, we sought to assess the effects of curcumin on the cardiac function in human models.

3. Methods

The present study was designed as a randomized, controlled, single-center clinical trial. The study was done with a pilot design in 2 groups of curcumin (n = 20) and placebo (n = 15). The sampling was done by placing the selected patients in 2 groups alternately. In other words, the 1st patient was placed in the curcumin group, the 2nd patient in the control group, the 3rd patient in the curcumin group, and so forth. The studied patients were all patients with chronic renal failure under dialysis. The age range was between 30 and 60 years. The exclusion criteria comprised a diagnosis of cardiac diseases such as coronary artery disease (based on coronary angiography or other noninvasive diagnostic tests), moderate-to-severe valvular heart disease, pregnancy and lactation, and refusal to give informed consent. The curcumin group received curcumin for 6 weeks at a dose of 500 mg every 8 hours (1500 mg/d), and the control group received a placebo drug at the same dose for 6 weeks. Before the start of treatment with curcumin and exactly after the 6th week, the patients underwent echocardiography and the ejection fraction (EF) representing LV function and size was measured for the 2 groups in the echocardiography department by echocardiologists. The time of echocardiography was 1 to 2 hours before dialysis.

3.1. Statistical Analysis

The obtained data were entered into IBM SPSS Statistics for Windows, version 21 (IBM Inc., Armonk, NY). The determination of the normal distribution of the quantitative variables was done via the one-sample Kolmogorov-Smirnov test. Then, the descriptive statistics of frequency, frequency percentage, mean, and SD were determined. The quantitative variables were compared between the 2 groups using the independent t-test. The χ^2 test or the Fisher exact test was employed to compare the qualitative variables between the 2 groups. The quantitative values were compared before and after angiography using the paired t-test. A $P < 0.05$ was considered statistically significant.

4. Results

The study population was comprised of 35 patients, divided into 2 groups of curcumin (n = 20) and placebo (n = 15). Ten patients were excluded due to their termination of cooperation, lack of data, or curcumin side effects.

The demographic data such as age, sex, and body mass index showed no significant differences between the 2 groups (Table 1). The levels of hemoglobin and parathyroid hormone exhibited insignificant differences between the 2 groups (Table 1). The duration of dialysis and the cause of renal failure had no significant differences between the 2 groups (Table 2).

The mean volume of the LV at end diastole in the curcumin group and the placebo group was 96.05 $\pm$ 16.39 cc and 104.67 $\pm$ 27.09 cc, respectively. The mean volume of the LV after drug administration was 96.05 $\pm$ 16.39 cc in the curcumin group and 104.67 $\pm$ 27.09 cc in the placebo group. The mean volume of the LV before and after intervention had no significant difference between the 2 groups. In addition, no significant difference was observed between the 2 groups before and after treatment (Table 3). LV diameter at end diastole was 4.94 $\pm$ 0.317 cm in the curcumin group and 5.25 $\pm$ 0.82 cm in the placebo group. The mean values for the curcumin and the placebo groups were respectively 4.84 $\pm$ 0.793 and 5.19 $\pm$ 0.591 cm. The mean values before and after intervention had no significant differences between the 2 groups. In addition, no significant difference was observed in the comparison of each group before and after treatment (Table 3, Figure 1). The EF before drug administration was 50.65% $\pm$ 7.06% in the curcumin group and 47.6% $\pm$ 8.58% in the placebo group. After the administration of the drug, the EF was 51.55% $\pm$ 6.84% in the curcumin group and 48.07% $\pm$ 7.06% in the placebo group. The mean value had no difference between the 2 groups before and after intervention. In addition, no significant difference was observed between the 2 groups before and after the intervention (Tables 3 and 4, Figure 1).

The comparison of average global longitudinal strain before and after intervention showed no significant difference between the 2 groups ($P > 0.05$), and nor there was there any significant difference in each group before and after intervention (Table 5).

Five patients in the curcumin group showed drug side effects. One of the patients had heartthrob, 2 of them had hypertension, 1 patient had shortness of breath, and the remaining patient had heartburn. These side effects gradually lessened as the treatment and administration of proton-pump inhibitors continued. In the control group,

Table 1. Patients' Characteristics

	Curcumin (n = 20)	Placebo (n = 15)	P Value
Age, y	44.15 ± 13.35	45.33 ± 6.17	0.735
Male, No. (%)	12 (60)	10 (66.7)	0.482
BMI, kg/m²	25.1 ± 6.54	25.64 ± 3.28	0.775
Hb, mg/dL	10.36 ± 1.08	10.13 ± 0.99	0.531
PTH, mg/dL	1911.09 ± 173.6	183.73 ± 167.4	0.901

Abbreviations: BMI, body mass index; Hb, hemoglobin; PTH, parathyroid hormone.

Table 2. Dialysis Data

	Curcumin (n = 20)	Placebo (n = 15)	P Value
Dialysis Duration, mo	15.05 ± 11.56	11.14 ± 5.27	0.247
Cause of Chronic Renal Failure	Diabetes mellitus: 40%	Diabetes mellitus: 40%	0.93
	Hypertension: 50%	Hypertension: 53.3%	
	Others: 10%	Others: 6.6%	

Table 3. Comparison of LVEDV and LVEDD Before and After Curcumin Administration

	Curcumin (n = 20)	Placebo (n = 15)	P Value
LVEDV before Curcumin Administration	97.1 ± 26.29	104.67 ± 27.09	0.412
LVEDV after Curcumin Administration	96.05 ± 16.39	102.93 ± 31.17	0.505
LVEDV within the Groups (P value)	0.137	0.302	-
LVEDD before Curcumin Administration	4.94 ± 0.317	5.25 ± 0.82	0.129
LVEDD after Curcumin Administration	4.84 ± 0.793	5.19 ± 0.591	0.157
LVEDD Within the Groups (P value	0.323	0.088	-

Abbreviations: LVEDD, Left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume.

Table 4. Comparison of LVEF (Diameter and Volume) Before and After Curcumin Administration

	Curcumin (n = 20)	Placebo (n = 15)	P Value
LVEF (volume) before Curcumin Administration	50.65 ± 7.06	47.6 ± 8.58	0.257
LVEF (volume) after Curcumin Administration	51.55 ± 6.84	48.07 ± 7.06	0.097
LVEF (volume) within the Groups (P value)	0.130	0.719	-
LVEF (diameter) before Curcumin Administration	51.85 ± 3.84	50.67 ± 7.28	0.538
LVEF (diameter) after Curcumin Administration	52.95 ± 3.55	51.33 ± 6.04	0.064
LVEF (diameter) within the Groups (P value)	0.112	0.375	-

Abbreviation: LVEF, Left ventricular ejection fraction.

4 patients had some drug effects. One of the patients had atypical chest pain, 1 had nausea, and the remaining 2 patients had heartburn. The side effects gradually decreased as the treatment continued and proton-pump inhibitors were administered. No dangerous or life-threatening events were observed in either of the groups (Figures 2 and 3).

Table 5. Comparison of Mean GLS and PAP Before and After Curcumin Administration

	Curcumin (n = 20)	Placebo (n = 15)	P Value
GLS Average before Curcumin Administration	-12.52 ± 2.87	-14.87 ± 2.86	0.099
GLS Average after Curcumin Administration	-13.15 ± 2.98	-15.94 ± 1.74	0.081
GLS Average within the Groups (P value)	0.114	0.216	-
Mean PAP before Curcumin Administration	39.85 ± 18.87	38.13 ± 7.82	0.743
Mean PAP after Curcumin Administration	38.45 ± 17.57	36.8 ± 8.15	0.306
Mean PAP within the Groups (P value)	0.067	0.375	-

Abbreviation: GLS, Global longitudinal strain; PAP, Pulmonary artery pressure.

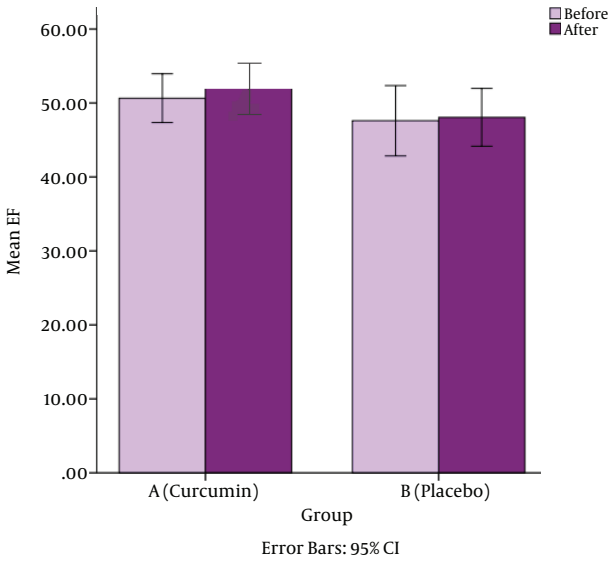

Figure 1. Comparsion of LVEF (Volume) Before and After Curcumin

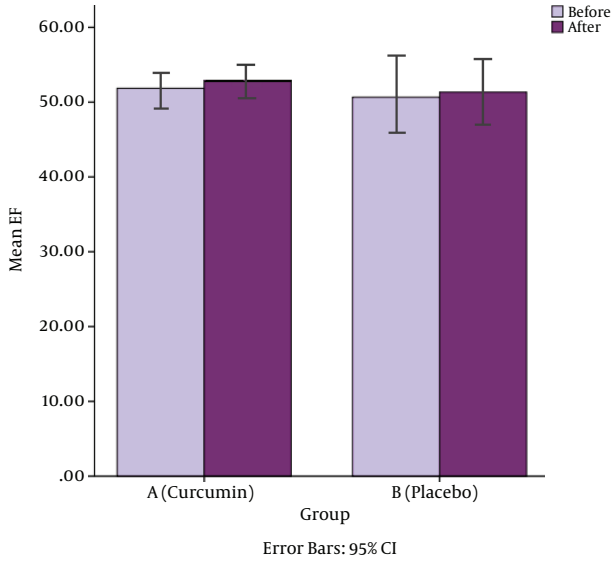

Figure 2. Comparsion of LVEF (Diameter) Before and After Curcumin

5. Discussion

The results of the present study indicated that curcumin had no significantly positive effects on increasing LVEF and decreasing LV volume. The comparison of the changes before and after treatment between the 2 groups and within each group showed no significant differences. The other echocardiographic indices associated with LV function did not present significant changes after the administration of curcumin inasmuch as average global longitudinal strain, representing the tissue velocity and myocardial function of the ventricle, did not indicate significant changes. In other words, the mean values obtained before and after treatment showed insignificant reduction in each group. Furthermore, curcumin had no positive effects on pulmonary artery pressure.

With respect to the side effects observed in the present study and the description of these conditions by the patients, it can be assumed that most of these effects may have been in consequence of gastrointestinal effects and gastroesophageal reflux (19-21). The fact that the side effects were observed in both groups and were similar suggests that curcumin had nothing to do with them and such effects were due to the side effects of other drugs.

Because the gastrointestinal absorption and bioavailability of curcumin are low, the reason for the ineffectiveness of curcumin in the present study may be its low dosage. In addition to the low dosage, the elimination of curcumin from the serums of the patients during dialysis might be another reason for this low serum level. Therefore, we suggest that further studies be conducted with higher doses of curcumin and usage of curcumin in a formulation which would offer better bioavailability. In addi-

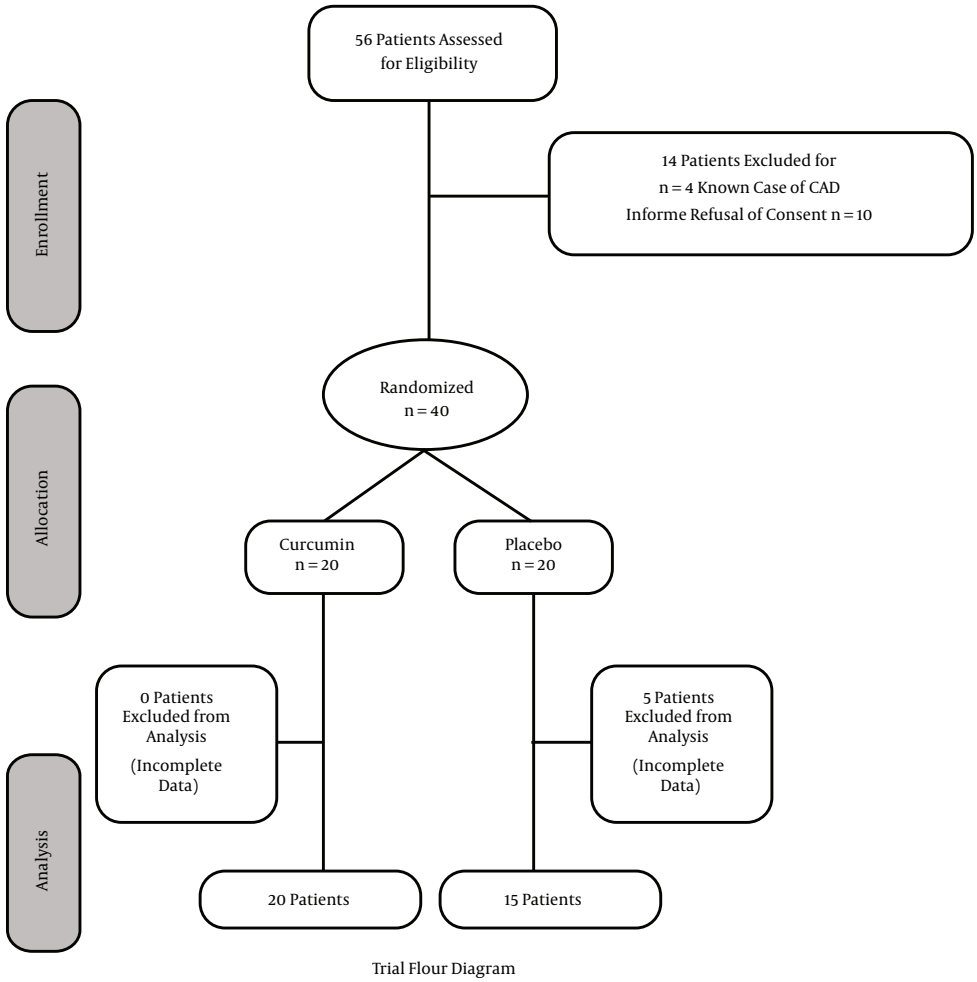

Figure 3. Trial Flow Diagram

tion, the effects of dialysis on the serum level of curcumin should also be probed into.

In light of the results of the present study indicating the ineffectiveness of curcumin in exerting positive effects on the LV, it seems advisable that studies with larger numbers of patients and more sub-group analyses be carried out with a view to arriving at more definite conclusions concerning the cardiovascular properties of curcumin in patients with chronic renal failure.

References

1. Fathi R, Isbel N, Haluska B, Case C, Johnson DW, Marwick TH. Correlates of subclinical left ventricular dysfunction in ESRD. *Am J Kidney Dis.* 2003;**41**(5):1016–25. [PubMed: 12722036].
2. Gross ML, Ritz E. Hypertrophy and fibrosis in the cardiomyopathy of uremia–beyond coronary heart disease. *Semin Dial.* 2008;**21**(4):308–18. doi: 10.1111/j.1525-139X.2008.00454.x. [PubMed: 18627569].
3. Salvetti M, Muiesan ML, Paini A, Monteduro C, Bonzi B, Galbassini G, et al. Myocardial ultrasound tissue characterization in patients with chronic renal failure. *J Am Soc Nephrol.* 2007;**18**(6):1953–8. doi: 10.1681/ASN.2006050462. [PubMed: 17442790].
4. Ireson CR, Jones DJ, Orr S, Coughtrie MW, Boocock DJ, Williams ML, et al. Metabolism of the cancer chemopreventive agent curcumin in human and rat intestine. *Cancer Epidemiol Biomarkers Prev.* 2002;**11**(1):105–11. [PubMed: 11815407].
5. Anand P, Sundaram C, Jhurani S, Kunnumakkara AB, Aggarwal BB. Curcumin and cancer: an "old-age" disease with an "age-old" solution. *Cancer Lett.* 2008;**267**(1):133–64. doi: 10.1016/j.canlet.2008.03.025. [PubMed: 18462866].
6. Kapakos G, Youreva V, Srivastava AK. Cardiovascular protection by curcumin: molecular aspects. *Indian J Biochem Biophys.* 2012;**49**(5):306–15. [PubMed: 23259317].
7. Ghosh SS, Salloum FN, Abbate A, Krieg R, Sica DA, Gehr TW, et al. Curcumin prevents cardiac remodeling secondary to chronic renal failure through deactivation of hypertrophic signaling in rats. *Am J Physiol Heart Circ Physiol.* 2010;**299**(4):975–84. doi: 10.1152/ajpheart.00154.2010. [PubMed: 20601462].
8. Wang NP, Wang ZF, Tootle S, Philip T, Zhao ZQ. Curcumin promotes cardiac repair and ameliorates cardiac dysfunction follow-

ing myocardial infarction. *Br J Pharmacol.* 2012;**167**(7):1550–62. doi: 10.1111/j.1476-5381.2012.02109.x. [PubMed: 22823335].
9. Duan W, Yang Y, Yan J, Yu S, Liu J, Zhou J, et al. The effects of curcumin post-treatment against myocardial ischemia and reperfusion by activation of the JAK2/STAT3 signaling pathway. *Basic Res Cardiol.* 2012;**107**(3):263. doi: 10.1007/s00395-012-0263-7. [PubMed: 22466958].
10. Sunagawa Y, Sono S, Katanasaka Y, Funamoto M, Hirano S, Miyazaki Y, et al. Optimal dose-setting study of curcumin for improvement of left ventricular systolic function after myocardial infarction in rats. *J Pharmacol Sci.* 2014;**126**(4):329–36. doi: 10.1254/jphs.14151FP. [PubMed: 25409899].
11. Chen TH, Yang YC, Wang JC, Wang JJ. Curcumin treatment protects against renal ischemia and reperfusion injury-induced cardiac dysfunction and myocardial injury. *Transplant Proc.* 2013;**45**(10):3546–9. doi: 10.1016/j.transproceed.2013.09.006. [PubMed: 24314955].
12. Kim YS, Kwon JS, Cho YK, Jeong MH, Cho JG, Park JC, et al. Curcumin reduces the cardiac ischemia-reperfusion injury: involvement of the toll-like receptor 2 in cardiomyocytes. *J Nutr Biochem.* 2012;**23**(11):1514–23. doi: 10.1016/j.jnutbio.2011.10.004. [PubMed: 22402367].
13. Gonzalez-Salazar A, Molina-Jijon E, Correa F, Zarco-Marquez G, Calderon-Oliver M, Tapia E, et al. Curcumin protects from cardiac reperfusion damage by attenuation of oxidant stress and mitochondrial dysfunction. *Cardiovasc Toxicol.* 2011;**11**(4):357–64. doi: 10.1007/s12012-011-9128-9. [PubMed: 21769543].
14. Carroll RE, Benya RV, Turgeon DK, Vareed S, Neuman M, Rodriguez L, et al. Phase IIa clinical trial of curcumin for the prevention of colorectal neoplasia. *Cancer Prev Res (Phila).* 2011;**4**(3):354–64. doi: 10.1158/1940-6207.CAPR-10-0098. [PubMed: 21372035].
15. Kumar S, Ahuja V, Sankar MJ, Kumar A, Moss AC. Curcumin for maintenance of remission in ulcerative colitis. *Cochrane Database Syst Rev.* 2012;**10**:008424. doi: 10.1002/14651858.CD008424.pub2. [PubMed: 23076948].
16. Chuengsamarn S, Rattanamongkolgul S, Phonrat B, Tungtrongchitr R, Jirawatnotai S. Reduction of atherogenic risk in patients with type 2 diabetes by curcuminoid extract: a randomized controlled trial. *J Nutr Biochem.* 2014;**25**(2):144–50. doi: 10.1016/j.jnutbio.2013.09.013. [PubMed: 24445038].
17. Ganjali S, Sahebkar A, Mahdipour E, Jamialahmadi K, Torabi S, Akhlaghi S, et al. Investigation of the effects of curcumin on serum cytokines in obese individuals: a randomized controlled trial. *ScientificWorldJournal.* 2014;**2014**:898361. doi: 10.1155/2014/898361. [PubMed: 24678280].
18. Morimoto T, Wada H, Sunagawa Y, Fujita M, Kakeya H, Imaizumi A, et al. Highly absorptive curcumin improves left ventricular diastolic function regardless of blood pressure in hypertensive patients. *J Am Coll Cardiol.* 2012;**59**(13) doi: 10.1016/S0735-1097(12)60988-7.
19. Van Dau N, Ham NN, Khac DH, Lam NT, Son PT, Tan NT, et al. The effects of a traditional drug, turmeric (Curcuma longa), and placebo on the healing of duodenal ulcer. *Phytomedicine.* 1998;**5**(1):29–34. doi: 10.1016/S0944-7113(98)80056-1. [PubMed: 23195696].
20. Hanai H, Iida T, Takeuchi K, Watanabe F, Maruyama Y, Andoh A, et al. Curcumin maintenance therapy for ulcerative colitis: randomized, multicenter, double-blind, placebo-controlled trial. *Clin Gastroenterol Hepatol.* 2006;**4**(12):1502–6. doi: 10.1016/j.cgh.2006.08.008. [PubMed: 17101300].
21. Epelbaum R, Schaffer M, Vizel B, Badmaev V, Bar-Sela G. Curcumin and gemcitabine in patients with advanced pancreatic cancer. *Nutr Cancer.* 2010;**62**(8):1137–41. doi: 10.1080/01635581.2010.513802. [PubMed: 21058202].