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Clinical efficacy of curcumin-based functional food mixtures for pain removal

[1,*]Huq, A.K.O., [1]Tama, A.A., [2]Mandal, A.K., [1]Uddin, I., [1]Talukder, M.U., [3]Abedin, N., [4]Zaher, M.A., [5]Ahmed, M. and [6]Haque, K.M.F.

[1]*Department of Food Technology and Nutritional Science, Mawlana Bhashani Science and Technology University, Tangail-1902, Bangladesh*
[2]*Organic Nutrition Limited, Banani, Dhaka-1213, Bangladesh*
[3]*Institute of Food Science and Technology, Bangladesh Council for Scientific and Industrial Research, Dhaka-1205*
[4]*Institute of Nutrition and Food Science, University of Dhaka, Dhaka-1000, Bangladesh*
[5]*Directorate General of Forces Intelligence, Dhaka Cantonment, Dhaka-1206, Bangladesh*
[6]*Integrated Nutrition and Health Research Center, Mohammadpur, Dhaka-1207, Bangladesh*

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Abstract

Functional foods have beneficial roles in health and well-being, beyond their basic nutrition. Nowadays, a lot of functional foods are emerging throughout the world. A curcumin-based functional food mixture (*Karkuma*) was formulated with a certain proportion of natural herbs and spices mixtures with the aim of alleviating pain. This was a three-month clinical trial conducted among a total of sixty patients with chronic pain (30 patients in the intervention and 30 patients in the control group). In the first phase, *Karkuma* was formulated by appropriately processing and blending mixtures of curcumin, gingerol, mulberry and multi-floral honey as the main ingredients. This formulation was standardized and sensory evaluated by a nine-point hedonic scale. The overall acceptable score was 8.1 (like very much) out of 9. The product safety and acute toxicity tests were tested in a renowned laboratory in Bangladesh and shown safe for consumption. In the second phase, these functional food mixtures claim to reduce the severity of pain and are thus evaluated by adjuvant therapy. No significant differences were found in both groups at baseline observation. After three months of intervention with *Karkuma,* significantly ($p<0.05$) relieves pain in the intervention group. However, no significant ($p>0.05$) decrease in pain was observed after three months of the control trial with blank *Karkuma.* Moreover, the hematological and liver function tests in both groups were at acceptable levels. Hence, this study acclaims the efficacy of functional food mixtures (*Karkuma*) against chronic pain.

1. Introduction

Progressively industrialization and economic development in developing countries significantly change their lifestyles and diets. As a result, having a major impact on the health and nutritional status of populations, especially chronic lifestyle diseases. Different types of pain, particularly chronic pain, are a common and severe condition for those who suffer from it, as well as the incapacity and psychological misery that comes with it. Furthermore, it is a huge worry, both for the individual and for the society as a whole, which bears the social and economic costs (Ehde *et al.,* 2003; Gatchel *et al.,* 2003; Hassett and Willians, 2011). A considerable number of individuals with chronic pain indicate that their pain is poorly controlled, causing them to miss work and interfering with daily activities (Vlaeyen and Linton, 2000). Pain is registered as the third leading reason for missing work (Chandra, 1996). Currently, Patients with chronic pain are treated in primary care with drugs which probably have a lot of side effects on the individuals. Again, patients' satisfaction with chronic pain management therapies is low to moderate. Despite substantial studies into chronic pain management and patient perceptions of chronic pain, little is known about the therapeutic and preventative properties of herbal combinations for pain relief management. However, Anesthesia, physical and occupational therapy, psychology, pharmaceutical management, and complementary and alternative medicine are among the treatment options available.

*Corresponding author.
Email: *akohuq@yahoo.com*

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Alternative medicine from natural herbs and spices has a long history of management of different pain and chronic diseases. Nutraceuticals are made up mostly of nutrients, herbals, and dietary supplements, which make them useful in maintaining health, fighting disease, and improving the overall quality of life (Keservani *et al.,* 2010). Therefore, nowadays, modern medicinal herbs and spices have been associated with a decreased risk of developing chronic diseases including pain relievers (Vázquez-Fresno *et al.,* 2019). The presence of phytochemicals and neutraceuticals bioactive functional components in herbs and spices are the main contributing factors for pain relief and in the human diet, these are not considered necessary nutrients. Curcumin, the yellow pigment found in the rhizome of turmeric (*Curcuma longa*), an ingredient in curry spice, has been shown to have antitumor, antiinflammatory, and anti-infectious properties, as well as inhibiting peroxidation. It is also used to treat toothache, diarrhea and epilepsy (Nwafor *et al.,* 2001; Bhat *et al.,* 2014). But they provide many health benefits such as anticancer, anti-inflammatory, antibacterial, antiviral and antioxidant effects (Lai and Roy, 2004; Steenkamp *et al.,* 2006; Shan *et al.,* 2007; Kaefer and Milner, 2008; Mueller *et al.,* 2010; Opara and Chohan, 2014). Curcuminoids were found to be much more effective in pain alleviation with no negative side effects (Hsiao *et al.,* 2021; Paultre *et al.,* 2021). It was discovered that turmeric extracts and curcumin treatment considerably reduced joint arthritis (Daily *et al.,* 2016) and was also linked to a reduction in knee osteoarthritis (Lopresti *et al.,* 2021). Some of them have been used in traditional medicine for healing and as health tonics or food supplements. Therefore, attempts have been made to formulate newly developed functional food mixtures and apply a clinical case-control study to gain a better understanding of the process of pain relief management through the patient's sign syndrome and, potentially, new approaches to service these patients for a better quality of life.

This study was also included to collect preliminary data for evaluating the overwhelming subjective claims of clinical efficacy of this mixture prior to the development of a placebo. The main outcome measures were clinical improvement, pain or inflammation severity reduction and inflammation duration. All adverse events were recorded, as well as laboratory studies, including hematological testing, to determine the safety and tolerability of functional food mixtures.

2. Materials and methods

The study was carried out in two phases.

2.1 First phase

Curcumin-based functional mixtures were formulated by the guarded secret ratio of several natural plant materials extracts including turmeric (*Curcuma longa*), ginger (*Zingiber olefera*), mullberry (*Morus alba*) and multifloral honey as main ingredients and standardized by organoleptic sensory evaluation test. The product quality was checked by the Functional Food Research Laboratory of Food Technology and Nutritional Science (FTNS) Department, Mawlana Bhashani Science and Technology University and heavy metals, microbiology and toxicological safety tests were done in the Bangladesh Council of Scientific and Industrial Research.

2.1.1 Sensory evaluation

In this study, eleven members of the panel evaluated the organoleptic characteristics of functional food mixtures on a “9 point Hedonic Scale” (Ranganna, 1986). The general form of the scale is: 1 (Dislike extremely) to 9 (Like extremely).

2.1.2 Hematological test and liver function test

The standard Westergren method was performed on sixty individual subjects for the determination of Erythrocyte sedimentation rate (ESR). A tube holding 0.5 mL of sodium citrate filled with 2 mL of blood, and the tube kept at room temperature (25°C) for 2 hrs. A Westergren-Katz tube is filled with blood up to the 200 mm mark. After an hour at room temperature, the tube is positioned strictly vertically in a rack, and the distance between the upper limit of the red cell sediment and the lowest point of the surface meniscus is measured. The distance of fall of erythrocytes, expressed as millimeters in 1 hr, is the ESR. The hemoglobin was measured by Sahli's Haemoglobinometer by a trained technician of the department of FTNS, in physiology Lab. The hemoglobinometer tube was first filled with N/10 HCl using a dropper to the lowest point, which is 2% or 10%. A finger prick was used to get the blood sample, which was then marked with a Sahli's pipette (20 µL), and then transferred to a N/10 HCl solution in a hemoglobin tube. After thorough mixing, let it sit for ten minutes to allow the hemoglobin to fully convert to hematin. Subsequently, drops of distilled water were added and swirled until the color of the mixture matched that of the comparator's reference glass. Obtaining the reading at the lower meniscus yields the hemoglobin concentration in 100 mL of blood. To carry out the Serum Glutamic Pyruvic Transaminase (SGPT) test, the serum was analyzed in Bayer's Express Plus, auto analyzer (Bayer Diagnostics, Siemens, USA). The enzyme, SGPT was quantitated following the method given by the manufacturer of the test kit with some modifications (Reitman and Frankel, 1957).

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2.2 Second phase

A randomized, single-blind placebo-controlled clinical trial was designed to observe the efficacy of the functional mixtures on the pain control of different types of selected pain patients. A total number of 60 chronic pain patients voluntarily joined this study and were randomly selected into two groups by their age and sex match. In each group, 30 individuals were included. All subjects in the intervention group were taking 15 mL formulated mixtures (*Karkuma*) twice daily for up to 3 months as an adjuvant therapy and in the control group taken a similar amount of blank *Karkuma* under the supervision of a physician. Furthermore, they were either using a single medicine or not. The severity of pain, types of pain, duration of daily pain, onset duration of pain, headache and presence of other pain-related complications were noted in the medical history of the patients.

This study was ethically approved by the Ethical Review Committee of the Department of Food Technology and Nutritional Science, Mawlana Bhashani Science and Technology University, Tangail, Bangladesh. If any case or control group patients would like to take functional food mixtures, the researcher asked for written consent from this study's participants. Moreover, if he or she becomes really ill with severe pain or any other complications, he or she might be treated with the required drugs under the supervision of a qualified specialist.

Inclusion criteria included ages between 40-60 years, as they are more prone to different types of pains. No gender bias and patients diagnosed with chronic pain. And also patients who have given written informed consent. Exclusion criteria were considered well-recognized rheumatoid arthritis pain, high blood pressure, and obesity grade III. Also excluded patients who take more than one drug and have debilitating illnesses.

The SPSS statistical program version 20.0 was used to analyze the data. The t-test with an acceptable significance level ($p<0.05$) was used to make comparisons in both groups.

3. Results and discussion

Herbal or food-based therapeutic mixtures are more appropriate for pain patients as it is traditionally and culturally accepted and can easily reach the majority of the population. Functional food mixtures (*Karkuma*) made with different natural herbal preparations are interventions in this study and are being found to be effective not only in changing the severity of chronic pain but also control other biochemical parameters in blood. Table 1 shows the organoleptic test of this newly developed functional product. The organoleptic test showed that the sample was highly acceptable.

Table 1. Sensory evaluation of the formulated functional food mixtures.

Quality factors	Points	Results
Color	8.36	Like very much
Flavor	7.54	Like moderately
Saltiness	8.27	Like very much
Hotness	7.81	Like moderately
Taste	7.90	Like moderately
Overall acceptance	8.09	Like very much

Table 2 also shows the respondent's opinion about regular consumption of provided functional food mixtures and indicated that it had good taste. About 13.3% of the subjects reported that it increased their appetite and the majority were interested in continued intake of this product. It was also observed that there are no adverse side effects such as hypersensitivity and gastrointestinal problems. The product safety and acute toxicity tests were tested in a renowned laboratory (Bangladesh Council of Scientific and Industrial Research) in Bangladesh. The heavy metal toxicity test report (S-1), microbiological safety test report (S-2) and acute toxicity test report (S-3) indicate the formulated functional foods (Karkuma) were safe for consumption and uploaded in supplementary attachments.

Table 2. Distribution of respondent's opinion about functional food mixtures (n = 30).

Opinion	Representative percent
Good taste	100.0
Standard amount of sweet	86.7
Standard amount of salt	83.3
Prefer to mix well	60.0
Increased appetite	63.3
Interested to take again	93.3
15-20 mL is adequate for each person per meal	93.3
Hypersensitivity	0.0
Gastrointestinal Problem	0.0

The sociodemographic and background characteristics of the sixty subjects who completed the study are shown in Table 3. The majority (50.0%) of them were between the ages of 40 and 49.9, while about one-third (31.7%) were between the ages of 50 and 59.9. The mean age in the intervention and control groups was 48.9 and 49.7 years, respectively. The age distribution in the control and intervention groups did not differ significantly. In both groups, there were no significant variations in weight, height, or body mass index (BMI).

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Table 3. Socio-demographic and background characteristics of subjects at day 0 (n = 60).

Variables	Intervention Group	Control Group	Total
	n (%)	n (%)	n (%)
Age			
40-49 Years	14(46.7)	16 (53.3)	30 (50.0)
50-59 Years	11 (36.7)	8 (26.7)	19 (31.7)
≥ 60 Years	5(16.7)	6 (20)	11(17.8)
Sex			
Male	12(40.0)	14 (46.7)	26 (43.3)
Female	18(60.0)	16 (53.3)	34 (56.7)
		Mean±SD	
Age (Years)	48.9±3.8	49.7±4.2	49.2±4.1
Weight (Kg)	64.7±4.5	66.5±5.4	65.6±4.9
Height (cm)	163.6±7.5	164.5±8.1	164.1±7.8
Body Mass Index	24.1±2.9	24.5±3.3	24.3±3.1
Mean duration of major pain (Years)	8.1±1.8	8.4±2.2	8.3±1.9

The distribution of pain felling by the respondents in the intervention and control groups at day zero and at 3 months after treatment with functional mixtures *Karkuma* (Table 4). There was similar severity of pain distribution was observed both in the intervention and control group at the baseline stage. After three months of intervention with *Karkuma* functional food mixtures, it was observed that there was a significant ($p<0.05$) reduces the severity of pain in the intervention group. None of them was found in the severe stage and 80% had no pain. On the other hand, in the control group no significant ($p>0.05$) decrease in the severity of pain after three three-month placebo control trials. Only slightly (13.3%) improves the severity of pain probably due to placebo effects.

Table 5 shows the distribution of hematological and liver function tests in both the intervention and control groups at baseline and after three months of clinical trials. It was noted that all the biochemical parameters were within the acceptable level and there were no significant changes or adverse effects in both two groups. This indicates that functional food health tonics are also safe for consumption. For the control and prevention of various types of pains, a variety of allopathic medications have been launched into the market. Traditional/herbal/alternative medications are becoming more popular in the treatment of many types of pain, mainly due to claims of minimal side effects. Curcumin-based Functional foods (*Karkuma*) are one such herbal food mixture, which is a natural herbal preparation and has been claimed to the lowering of the severity of chronic pain.

4. Conclusion

The formulated functional food mixtures (*Karkuma*) were good in taste without any hypersensitivity or gastrointestinal problems. The clinical efficacy of this *Karkuma* food was used as a customary anti-inflammatory agent to control pain relievers significantly. It was also delineated that within the period (3 months) of this study it did not cause any hepatotoxicity or hematological toxicity, thereby suggesting that it is safe within the limits of the tested parameters.

Table 4. Comparison of the severity of pain at baseline and after three months intervention in both groups.

Parameters	Intervention group			Control Group		
Pain Scale (0-10)	At baseline n (%)	After 3 months n (%)	p-value	At baseline n (%)	After 3 months n (%)	p-value
No Pain (0)	0 (0.0)	24 (80.0)		0 (0.0)	0 (0.0)	
Mild (1-3)	0 (0.0)	4 (13.3)		0 (0.0)	3 (10.0)	
Moderate (4-6)	8 (26.7)	2 (6.7)	$p<0.05$	9 (30.0)	10 (33.3)	$p>0.05$
Severe (7-10)	22 (73.3)	0 (0.0)		21 (70.0)	17 (56.7)	
Total	30 (100)	30 (100)		30 (100)	30 (100)	

Table 5. Distribution of the hematological and liver function tests at baseline and after three months intervention in both groups.

Biochemical parameters	Intervention group		Control Group		Standard value
	At baseline M±SD	After 3 months M±SD	At baseline M±SD	After 3 months M±SD	
ESR	18.1±3.3	17.2±3.1	18.7±3.2	18.2±2.9	<20
Hemoglobin (mg/dL)	10.9±1.3	10.8±1.3	10.8±1.4	10.5±1.3	>11.0
SGPT (U/L)	17.1±4.3	13.9±3.8	18.3±4.5	19.1±4.3	Up to 40

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Conflict of interest

The authors declare no conflict of interest.

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