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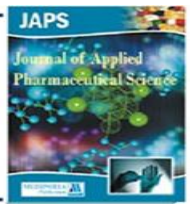

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Effects of 6-weeks water-based intermittent exercise with and without *Zingiber officinale* on pro-inflammatory Markers and blood lipids in Overweight Women with Breast Cancer

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ABSTRACT

Overweight and obesity is a risk factor for breast cancer. In contrast, physical regular activity has been suggested to help increase the survival of individuals with breast cancer. However, few studies have assessed effect of individually and combined *Zingiber officinale* (as a anti-inflammatory factor) with water-based exercise on the pro-inflammatory markers and blood lipid levels in overweight women with breast cancer and results have been inconsistent. The aim of this study was to determine the individual and concomitant effect of 6-wks water-based exercise and oral *Zingiber officinale* supplement on the aforesaid markers in overweight women with breast cancer. Forty women diagnosed with breast cancer(48±5.4 years, 76±9 kg, fat mass 41.8±4 %), volunteered to participate in the study. Subjects were randomly assigned into four groups; placebo, water-based exercise, *Zingiber officinale* and water-based exercise + *Zingiber officinale* groups. Subjects in the *Zingiber officinale* group and the exercise training+ *Zingiber officinale* group orally received 4 capsules (each capsule contained 750 mg), 7 days a week and for 6 weeks. The water-based exercise program were collected at a progressive intensity and time, ranged from 50% to 75% of heart rate reserve, in a pool with 15 meters width, 4 times a week for 6 weeks. Fasting blood sampling was collected at the pretest and post-test. The *Zingiber officinale* supplementation and or the water-base exercise resulted in a reduction of hs-CRP, IL-6 and TG, as compared to pretest. However, the combined intervention (water-base exercise and *Zingiber officinale*) group showed significantly a far better effect on the markers of pro-inflammatory and blood lipids, as compared to the water-base exercise or *Zingiber officinale* supplement alone groups and the age-matched placebo group. Our findings indicate a protective effect of the nondrug strategies such as water-base exercise and anti-inflammatory herbal factors such as; *Zingiber officinale* in the pathogenesis of inflammatory and metabolic responses in overweight women diagnosed with breast cancer.

Keywords: Overweight, Breast cancer, *Zingiber officinale*, Water-base exercise, Systemic inflammation.

INTRODUCTION

Cancer is one of the leading causes of death worldwide, accounting for 13% of all deaths, equivalent to 7.4 million people per year (Barbaric*et al.*, 2010). Women with a family history of breast cancer have a two to four times increased risk for developing breast cancer (BC) (Sheri *et al.*, 2011). Despite the prevalence of breast cancer, the majority of women are surviving and facing the task of combating the physiological and psychological problems resulting from cancer and its treatment (Lisa *et al.*, 2010).

Chemotherapy is commonly used as an adjuvant treatment to reduce the likelihood of metastasis (Lisa *et al.,* 2010). While cancer itself is a life-threatening disease, treatments for cancer such as Chemotherapy, can produce very unpleasant complications and side effects, including fatigue, anxiety, menopausal symptoms, nausea, lymphedema, and dermatitis. Such complications result in poor psychological adjustment, vitality status and quality of life (Lai Yi *et al.,* 2010; Deborah *et al.,* 2010). Similarly, depression increases in the first year after breast cancer diagnosis, and increased depression following breast cancer diagnosis is positively correlated with mortality (Lisa *et al.*, 2010).

Physical inactivity and a sedentary life style are associated with elevated inflammatory markers (Willem *et al.*, 2008). Low levels of physical activity, together with obesity, are associated with one-third to one-fifth of all colon, breast, kidney, and digestive cancers (World Health Organization, 2009). In contrast, research has consistently found an inverse relationship between regular physical activity and breast cancer risk (Sheri *et al.,* 2011; McTiernan, 2008, Phipps*et al.,* 2011). In addition to the direct benefits of physical activity on breast cancer, physical activity can also reduce adiposity (Sheri *et al.,* 2011; Donnelly *et al.,* 2009), which is associated with increased risk of lifetime breast cancer in postmenopausal women (Patterson *et al.*, 2010; Renehan *et al.,* 2008). According to the World Health Organization (WHO), regular physical activity is among the nine modifiable risk factors for cancer (World Health Organization, 2009). Furthermore, physical activity has previously been found to be a valuable rehabilitation tool for cancer survivors during treatment (Sheri*et al.,* 2011). Also, exercise interventions implemented concurrent with breast cancer treatment can cause increase in cardiovascular fitness, muscular strength, and body composition and decrease in cancer-related fatigue (Sheri *et al.*, 2011; Carole *et al.*, 2007).Although, various researchers reported water-based regular exercise is an ideal form of exercise for obese patients and may provide an attractive alternative to land-based exercise for achieving improved health and fitness in these populations (Kim *et al.*, 2011; Davidson *et al.,* 2000), aerobic exercise, particularly in attractive and buoyant environments such as, pools in overweight women following chemotherapy and completion of breast cancer treatment is poorly understand.

On the other hand, increasingly evidence indicates that herbal therapy is effective in alleviating anxiety, lessening cancer treatment-related side-effects, and facilitating rehabilitation (Lai Yi *et al.,* 2010). *Zingiber officinale*, has been used in Ayurvedic and Chinese medicine for the treatment of asthma, diabetes, nausea, pain and inflammation(Younget al., 2005,Thomsonet al., 2002). In vitro investigations show that ginger and several of its chemical constituents, including gingerols, shogaols, paradols, and zingerone, block the production of interleukins, and inflammatory markers (Lantz *et al.,* 2007; Thomson *et al.,* 2002). Therefore, ginger seems has a potentially important role in inhibit inflammatory process in cancer patients. In addition, role of oral ginger consumption as an anti-inflammatory factor or pain reliever in humans has not been sufficiently studied. However, little research is available to our understandingabout the efficacy of oral *Zingiber officinale* on pro-inflammatory parameters in overweight women suffering from breast cancer.

Therefore, with respect to situation of these patients who need an exhilarating milieu and the effect of physical activity in attractive environments like buoyant milieu, the first purpose of this study was to determine the individual and concomitant effect of six-weekswater-based intermittent exercise in the pool and oral *Zingiber officinale* on pro-inflammatory markers such as; high sensitive C-reactive protein (hs-CRP) and interloukine-6(IL-6),in overweight women suffering from breast cancer. In addition, given the relationship between inflammation and blood lipids, the second purpose of this research was to investigate the blood lipids alterations such as; triglyceride (TG) and total cholesterol(TC)that occur as a result of six-weeks intermittent water-based exercise and oral *Zingiber officinale* interventions in breast cancer survivors.

MATERIALS AND METHODS

Subjects and Selection procedure

The current study included 40 women, mean fat mass 42± 4 % , weight 76± 9 kg, height 156± 5 cm age 48±6 years, BMI 32±4 kg/m^2, diagnosed with breast cancer. All participants had completed radiation and/or chemotherapy treatments.After expressing an initial interest in the investigation, each potential participant met with the study coordinator, was screened for inclusion criteria using a brief eligibility checklist, and learned about the details of the study including assessment and training program. Participants were informed of thevoluntary and confidential nature of the study and were free to discontinue at any time. Informed consentwas obtained before participation in the study.Participants received comprehensive screening followedby an initial medicalexamination before theywere included in the study.

Inclusion and exclusion criteria

Eligibility criteria included a primary diagnosis of breast cancer during stage I–II, no distant metastases, ≥40 years old, completed radiation and/or chemotherapy treatments. Furthermore, women were excluded if they had evidence of recurrent disease, had previously engaged in any formal exercise programs for at least six months prior to participation in this study. Also, according to medical examinations, the subject don't have any cardiovascular and diabetic diseases. In addition, they did not smoke at least six months before the study began.

Study Design

The experimental protocol of current study was approved by Department of Physiology, University of Mazandaran. Subjects were randomly divided into four groups consist to; 1) placebo, 2) exercise training, 3) *Zingiber officinale* and 4) exercise training+ *Zingiber officinale* groups(10 cases in each group). Patients in the placebo group were instructed not to begin any new formal physical exercise program during the study intervention period.

All patients underwent a series of baseline assessments. The subjects' anthropometric variables included height, age, body mass, percent of body fat, lean body mass, and body mass index (BMI) were assessed. After completing all baseline assessments, patients were performed individually prescribed exercise with and without oral *Zingiber officinale* interventions.

Familiarization andwater-based intermittent exercise protocols

Subjects in the placebo and *Zingiber officinale* groups did not participate in any exercise program. However, each subject in the exercise training groups(exercise training group and exercise training+ *Zingiber officinale* group) participated in four familiarization sessions. For the subjects in the aforesaid training groups, a pool exercise training program was implemented and subjects were instructed to begin with an individually determined number of training sets and repetitions at adetermined intensity during first week.Each exercise session was individualized for the cancer survivor but generally included a 10 minute warm up, 20-60 minutes of aerobic exercise in water and concluded with a 10-minute cool down.

Deep-water exercise protocol was defined as those in which participants had no foot contact with the bottom of the pool.The upright water-based exercise training programwas performed in a pool with 15 meters width and 4 meter depth, as was described by Kim *et al.*, 2011.This exercise program was implemented for 6 weeks and 4 sessions at a week. The training groups were divided to the various subgroups and in each subgroup, those who had similar cardio-respiratory fitness, swimming in the water with equal intensity and rhythm. The distance of exercise was increased gradually with regard to over load principle, the training sets and training cycle. Exercise intensity was based on the cancer survivors' treadmill assessment results, and ranged from 50% to 75% of heart rate reserve (HRR). The Karvonen method or percentage of HRR was used to determine exercise heart rate intensity by using the formula (exercise target heart rate = [max HR - rest HR] × % exercise intensity + rest HR (Carole *et al.*, 2007).

After every set, the exercise intensity was controlled with pulse rate. On the average, the subjectsswimming every 30-meter distances with aforesaid intensity in 50 to 60 seconds. The recovery time between every walking was 30 to 40 seconds. The rests time between the sets was 5 to 6 minutes in order to allow heart rate to return to primary situation. Generally, the participants exercised two sets daily during the first week, but for the next weeks, they exercised three sets daily. In addition, the number of repeats of swimming in the pool with 30-meter length from the first week until the 6th week was 34, 75, 24, 92, 112 and 131, respectively. The subjects in the training groups swimming a total of 14,850 meters during 24 sessions of pool swimming.

***Zingiber officinale* supplementation procedure**

Subjects in the *Zingiber officinale* group and the exercise training+ *Zingiber officinale* group orally received 3 capsules (Each capsule contained 750 mg) of Zingiber rhizome powder(Goldaroo. Company, Tehran, Iran), 7 days a week and for 6 weeks, consistent with previous studies (Christopher *et al.*, 2010). The subjects consumed the powder in approximately 250 ml of water. The supplement was ingested 4 times a day, with breakfast, lunch, dinner and afternoon. The placebo group received capsules contained 1 gr starch (placebo), in the same manner and for the same duration of time as the experimental groups. Subjects during the supplementation period, maintain their normal food program and recommended them to refrain from consuming any antioxidants and multivitamins-containing substances, with the exception of tamoxifen drug.

Blood sampling and Biochemical analysis

Blood samples were collected from each subject at pretest and at the end of 6 weeks of water-based exercise with and without *Zingiber officinale* in an overnight 10 to12-h fasting state. A 5mL blood sample was collected via venipuncture of an antecubital vein. The blood samples were allowed to clot at room temperature for 10 min and then centrifuged(10 min at 5°C, 3,000 g).The serum was then pipette into polystyrene tubes. The aliquots were frozen at −80°C for subsequent assays.The hs-CRP concentration was determined by Latex particle-enhanced, as described by Roshan *et al.*, 2011. In summary, immunoturbidimetric assay on a Hitachi 912 automated analyzer using reagents from Diasorin (Stillwater, Minnesota). The high-sensitivity C-reactive protein concentration was determined from CRP standards of known concentration. Also, IL-6 was measured by a high sensitive Quantikine assay, as described by dabidi Roshan et al (Dabidi *et al.*, 2011). Furthermore, Triglycerides (TG), total cholesterol (TC), were measured using by enzymatic assays.

Statistical analysis

Statistical analysis was performed using a commercial software package (SPSS version 16.0 for Windows). Results are expressed as means ± SE. Dependent t-test was used to determine the changes of the pro-inflammatory markers and blood lipids between pre-test and post-test in experimental groups. In addition, one-way ANOVA was used to detect statistical differences between the four groups. Post-Hoc tests (Tukey) were performed to establish differences in the pro-inflammatory markers and blood lipids between groups. Differences were considered significant at $p<0.05$.

RESULTS

Body composition and anthropometric characteristics of the subjects at the beginning of the research are presented in Table 1. No differences existed in age, height, body mass, body mass index and fat mass between four groups (table 1).

Pro-inflammatory markers

Changes in CRP and IL-6 in overweight women with breast cancer in each group are shown in Table 2. Six weeks of the *Zingiber officinale* in doses of 3 gr per day was beneficial in alleviating the systemic inflammation, so that, it resulted in a reduction of hs-CRP andIL-6 (34%, 41%, respectively), as

compared to before 6-wk of *Zingiber officinale*. However, in the sedentary placebo (control) group, the aforesaid markers levels remained unchanged, as compared to pretest.In addition, 6-wk of the water-base intermittent exercise cause a reduction of hs-CRP andIL-6, (24%, 29%, respectively), in comparison to before 6-wk of the water-base exercise.

However, the water-base exercise+*Zingiber officinale* treatment was more effective than the water-base exercise and the *Zingiber officinale*, alone treatment, such that, it led to a reduction of hs-CRP andIL-6(47%, 42%, respectively), in comparison to before 6-wk of treatment (table 2). However, the *Zingiber officinale* resulted in a significant decrease in hs-CRP ($p<0.001$) and IL-6 ($p<0.001$) Levels, in compared to the placebo group. Also, significant decreases in hs-CRP and IL-6 Levels were present not only in the water-base exercise group ($p<0.01$and $p<0.001$, respectively), but decreases were also observed in the water-base exercise+*Zingiber officinale* group($p<0.001$ and $p<0.001$, respectively), as compared to sedentary control group. However, after 6-wk of training, hs-CRP and IL-6 levels did not differ from that observed in the *Zingiber officinale* group ($p=0.544$ and $p= 0.572$, respectively). The combination of water-base exercise and *Zingiber officinale* has a far better effect on the markers of pro-inflammatory rather than using each of them separately (fig 1 and 2).

Table. 1: Characteristics of anthropometric and body composition in the various groups.

Parameter and groups	Placebo	water-base exercise	Zingiber	Zingiber+water-base exercise	P-value
Age(year)	50.4±3.4	47.3±8.1	46.4±5.5	47.5±4.6	0.434
Height(cm)	156±4.9	157±6.7	157±4.6	156±4	0.949
Body Fat(%)	42.48±3.9	40.52±5.5	39.2±3.9	40.1±3.3	0.381
Weight(kg)	74.27±10.9	71.36±4.9	77.61±7.5	74.74±9	0.435
BMI (kg/m²)	32.77±2.9	29.78±3	32.18±2.9	31.26±5.1	0.289

Values expressed as means±SD, Abbreviation; BMI (body mass index).

Table. 2: The pro-inflammatory Markers and blood lipids in before and afterwater-base exercise and Zingiberofficinale interventions.

Variable	Placebo			water-base exercise			Zingiber			Zingiber+water-base exercise		
	pre	post	P	pre	post	P	pre	post	P	pre	post	P
CRP	3.78±.77	3.88±.85	.844	3.80±1.09	2.88±.52❋#	.059	3.75±95	2.48±.64❋	.002	3.80±.89	2.02±.57❋	.001
IL6	5.30±.92	5.40±1.11	.852	5.17±1.3	3.65±.75❋	.020	5.27±1	3.12±.72❋	.000	5.13±.98	2.97±1❋	.002
TC	210±48.7	213±30.9	.717	201±25.5	191±19.6	.300	181±39.2	192±19.3	.514	195±74.9	185±25.4	.654
TG	147±23.1	139±22.6	.381	138±28.2	117±14.9	.031	148±26.6	146±35.7	.851	145±23.1	11613.8	.003

Data are presented as the mean±SD for 10 subjects; Abbreviation; CRP (C reactive protein), IL-6 (interleukin 6), TC (total cholesterol) and TG (triglyceride). ❋significantly different from placebo group($p<0.001$), # significantly different from combined (Zingiber+exercise) group ($p<0.01$).

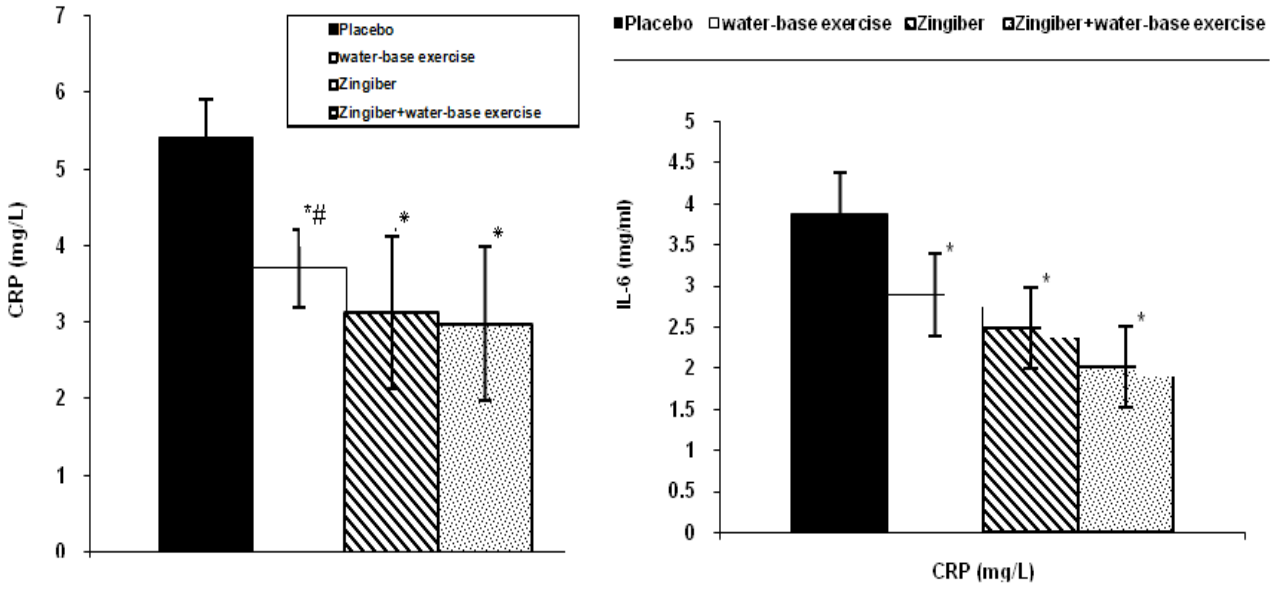

Fig. 1: Level of the pro-inflammatory Markers during water-base exercise with and without *Zingiberofficinale* interventions. Data are presented as the mean±SD for 8 Rats;Abbreviation; CRP (C reactive protein), IL-6 (interleukin 6). *significantly different from placebo group ($p<0.001$), # significantly different from combined (Zingiber +exercise) group ($p<0.01$).

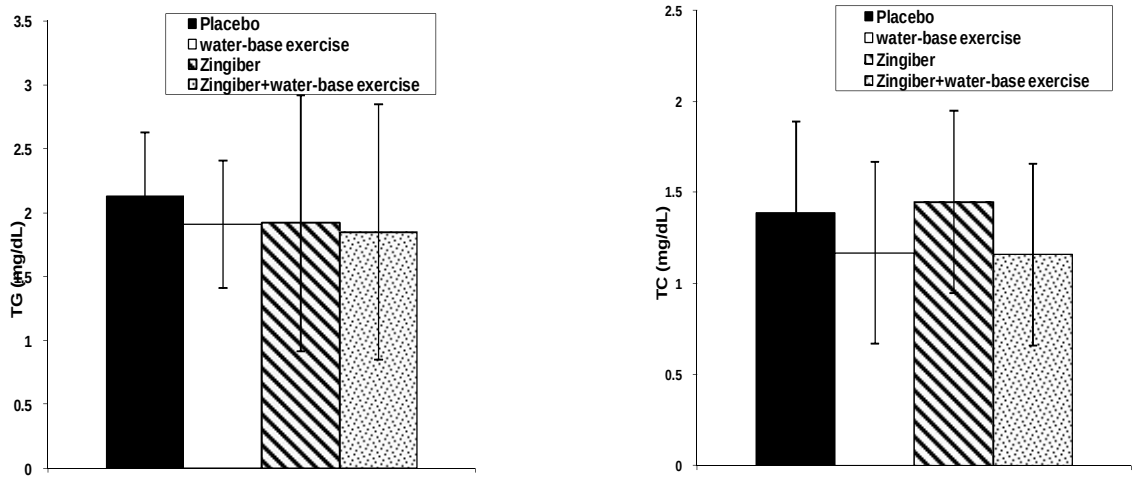

Fig. 2: Level of the blood lipids during water-base exercise with and without Zingiberofficinale interventions. Data are presented as the mean±SD for 8 Rats;Abbreviation; TC (total cholesterol) and TG (triglyceride).

Blood lipids

Table 3 show changes in the blood lipids (TC, TG) in overweight women with breast cancer in each group. 6-wk of the *Zingiber officinale* supplemention doses of 3 gr per dayresulted in a reduction of TG (2%) and a increase in TC (6%), as compared to before 6-wk of *Zingiber officinale*. However, in the sedentary placebo (control) group, TG and TC levels remained unchanged, as compared to pretest. In addition, 6-wk of the water-base intermittent exercise cause a reduction of TC and TG (4.5% and 15%, respectively), in comparison to before 6-wk of the water-base exercise. However, the water-base exercise+ *Zingiber officinale* treatment was more effective than the water-base exercise and the *Zingiber officinale*, alone treatment, so that, it led to a reduction of TC and TG (5% and 20%, respectively), in comparison to before 6-wk of treatment (table 2).However, significant difference in the TG levels was detected between the *Zingiber officinale*, as compared to the water-base exercise group and the combined group(p=0.048 and 0.038, respectively)(fig 1).

DISCUSSION

This study was designed to determine whether 6 weeks of water-based exercise with and without *Zingiber officinale* would influence the pro-inflammatory markers and blood lipids in obese women with breast cancer. The primary novel finding in present study was that consumption of *Zingiber officinale* in doses of 3 gr per day was beneficial in alleviating the systemic inflammation (hs-CRP and IL-6), while it has not significant effect on total cholesterol (TC) and triglyceride (TG). On the other hand, 6 weeks of water-based exercise cause significant decrease in hs-CRP, IL-6 concentration and insignificant reduce in TC and TG levels, as compared to control (placebo) group. However, The main findings of our study was that water-based exercise with *Zingiber officinale* significantly attenuated systemic inflammation and blood lipids in overweight women with breast cancer, as compared to the other groups. These findings are consistent with data from randomized controlled trials that reported reduction in blood lipids (Meredith *et al.*, 2009; Gappmaier *et al.*, 2006; Volaklis *et al.*, 2006), glucose and insulin response (Kim *et al.*, 2011; Volaklis *et al.*, 2006) and improve in cardiovascular health (Kim *et al.*, 2011; Meredith *et al.*, 2009; Chu, 2004; Volaklis *et al.*, 2006; Takeshima *et al.*, 2002) following aerobic exercise in water versus walking/or running on land in older, overweight women. However, the available studies using upright water-based exercise interventions are limited and the methodological limitations of these studies should be considered when assessing their findings. Moreover, findings obtained in land-based exercise training studies cannot be simply extrapolated to aquatic activities. Overall, non-weight bearing exercise is recommended by the American College of Sports Medicine (ACSM) as a possible alternative to improve health and well-being for individuals who find weight bearing exercise difficult (Kim *et al.*, 2005).

Overall, previous researchers reported participation in the regular physical activity improves rates of breast-cancer survival. Although the exact mechanism through which the regular physical activity may affect breast-cancer survival is unknown, a few possible hypotheses exist. The regular physical activity may influence prognosis by similar mechanisms to those thought to prevent the incidence of breast cancer, including decreased lifetime estrogen exposure and improved immune function (Barbaric *et al.*, 2010). Increased physical activity also reduces insulin resistance and hyperinsulinemia. Furthermore, lower blood-estrogen levels, higher insulin growth factor–I concentration, and lower levels of fatty tissue have all been associated with participation in physical activity. Reductions in blood-estrogen levels have been associated with decreased proliferative activity in breast tissue (Barbaric *et al.*, 2010).

Weight increase and obesity have been identified as the most important risk and prognostic factors for breast cancer in women. Several hypotheses have been proposed to explain the association of obesity with breast cancer. A hypothesis is that obesity, results in increased circulating levels of the pro-inflammatory markers and blood lipids. Specific obesity-associated factors, including blood lipids, insulin and inflammatory mediators, seem to influence breast cancer growth and prognosis independently of estrogens (Antonio *et al.,* 2011). Our study shows that pro-inflammatory cytokines such as; CRP and IL-6 was elevated in breast cancer survivors. In contrast,6 weeks of water-based exercise resulted in decrease in IL-6 and hs-CRP concentration, as compared to control group. Pro-inflammatory cytokines are produced as acute phase proteins by the liver, and may provide a more accurate reflection of cytokine activity (Julienne *et al.,* 2009). Thus, the aforesaid markers may be more reliable and sensitive indicators of systemic inflammation. IL-6 is a known pro-inflammatory cytokine secreted by activated macrophage and involved in several functions of the immune response that exerts also various metabolic and endocrine activities. It has been demonstrated that IL-6 increases following menopause in healthy women(Morley 2004). Furthermore, Antonio et al (Antonio 2011) reported IL-6 may be associated with breast cancer through several mechanisms, including regulation of insulin, inflammation, and estrogen, all factors that may significantly influence the evolution of this disease (Antonio, 2011). In fact, pro-inflammatory cytokines could facilitate tumour growth and metastasis by altering tumour cell biology and activating stromal cells, tumour-associated macrophages and fibroblasts (Cole *et al.,* 2009). Moreover, systemic chronic inflammation mediated by IL-6 may increase the risk of breast cancer recurrence and affect its prognosis (Pierce *et al.,* 2009). Also, researchers have focused on a variety of factors that may potentially influence inflammatory responses. These factors include age, gender, repeated bouts of eccentric exercise, antioxidant supplements, intracellular calcium homeostasis, and anti-inflammatory drugs (Davidson *et al.,* 2000).

To date, no randomized clinical trials have investigated the interactive effect of water-based exercise and *Zingiber officinale* among overweight women diagnosed with breast cancer. Despite this, results from the few studies that have investigated the effects of water-based training on blood lipid profiles have been inconsistent. Twelve weeks of shallow water circuit training has been reported to significantly reduce TC (5—11%) and LDL-C (7—17%) levels with no significant change in HDL-C or TG in older women71 or middle aged, overweight women Our study shows that consumption of *Zingiber officinale* has not significant effect on total cholesterol (TC) and triglyceride (TG). Also, 6 weeks of water-based exercise resulted in insignificant reduce in TC and TG levels, as compared to control (placebo) group. However, water-based exercise with *Zingiber officinale* significantly attenuated blood lipids in overweight women with breast cancer, as compared to the other groups.The lack of change in lipids after chronic water-based training is disagreement with the effects of pro-inflammatory markers. The discrepant results may be due to the duration of the training programs enlisted (6 weeks vs 12 weeks), the intensity of the training program, or the baseline lipid status of the participants. Thus, the available evidence is not consistent with the idea that regular water-based exercise is associated with favourable changes in any lipid parameter (Kim *et al.,* 2011).

According to the present study, *Zingiber officinale* in overweight women with breast cancer resulted in lower levels of inflammation following consumption of 6 weeks in doses of 3 gr per day, as compared to before the supplementation period and compared to control group. *Zingiber officinale*, commonly known as ginger, has been used in Ayurvedic and Chinese medicine for the treatment of asthma, diabetes, nausea and pain (Christopher *et al.,* 2010). The dried rhizomes of Zingiber (rich in pungent phenolic compounds: gingerols and shogaols) or extracts thereof are important ingredients of many traditional/ alternative medicines worldwide (Gamal *et al.,* 2011). Furthermore, ginger has been shown to inhibit the release of pro-inflammatory cytokines in vitro. These established biological actions suggest that ingested ginger could blunt the increase in mechanical hypersensitivity of muscle tissue via a reduction in direct activation of type III and type IV afferent nerve fibers by substances such as bradykinin and sensitization of afferent fibers by prostaglandins and cytokines such as IL-1 and IL-6 (Thomson *et al.,* 2002). Also, modern science has revealed that turmeric curcuminoids inhibit inflammation by blocking the adhesion of monocytes to endothelial cells through inhibiting the activation of the cell surface adhesion molecules. Moreover, they suppress inflammation by inhibiting the nuclear factor-κB activation, which leads to inhibition of gene expression of pro-inflammatory cytokines, chemokines and cyclooxygenase (COX)-2 as well as osteoclastogenesis.Gingerols can also inhibit the synthesis of inflammatory mediators such as PG and leukotrienes in vitro. In addition, ginger extract was found to inhibit beta-amyloid peptide-induced cytokine and chemokine expression in cell line of human monocytes (Gamal *et al.,* 2011). The question of whether ginger has large effects on pain in women with breast cancer will be best addressed by future studies that use the same scale to assess pain perceptions.

In conclusion, 6 weeks of water-based intermittent exercise would influence the pro-inflammatory markers in obese women diagnosed with breast cancer. Furthermore, our findings show that water-based exercise with *Zingiber officinale* attenuated systemic inflammation and blood lipids in overweight women with breast cancer. These results suggest that water-based exercise with oral *Zingiber officinale* may have a more anti-inflammatory effect. Moreover, herbal therapy seems to offer a useful complementary treatment that can enhance the health outcome of this group of patients.

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