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DOES THE WHOLE BODY VIBRATION ALTER THE EFFECT OF A CORIANDRUM SATIVUM EXTRACT ON THE BIODISTRIBUTION OF THE RADIOPHARMACEUTICAL TECHNETIUM-99M SODIUM PERTECHNETATE AND SOME BIOMARKERS IN WISTAR RATS?

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Coriandrum sativum extract, radiopharmaceutical, serum biomarkers, vibration generated in platform

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Laboratório de Radiofarmácia Experimental, Departamento de Biofísica e Biometria, Instituto de Biologia Roberto Alcantara Gomes, Universidade do Estado do Rio de Janeiro, Avenida 28 de Setembro, 87, 20551030, Rio de Janeiro, Brazil E-mail: ericfrederico@msn.com **ABSTRACT:** The exposure to vibrations generated in oscillating/vibratory platform produces whole body vibration (WBV) exercises. The effect of the WBV in the concentrations of some biomarkers and his association between some substances has been investigated. Natural products have been used by the humans as food source and as medications. Coriandrum sativum (CS) is used for the treatment of diabetes and gastrointestinal complications. The aim of this study was evaluate if the WBV modify the effect of a CS on the biodistribution of Na^{99m}TcO₄ and in some biomarkers in Wistar rats. Rats were divided in: control group (CON) received of 0.9% NaCl solution (saline); treated group with 1.0 mL CS 8g/mL (COR); PLA were submitted to WBV (12 Hz) and also received 1.0 mL of saline; COR + PLA received 1.0 mL CS 8g/mL and were submitted to WBV. Na^{99m}TcO₄ was administrated via ocular plexus. After 10 min, sample of blood obtained from by cardiac puncture was used for biochemical analysis and organs isolated to determine %ATI/g. %ATI/g had a significant (p<0.05) alteration in spleen. Related to the biomarkers, significant (p<0.05) alterations were found in concentrations of the cholesterol, triglyceride, alkaline phosphatase, bilirubin and CK. Putting together all the findings reported in this investigation, the results indicated that the treatment with the association of an extract of CS and WBV (12 Hz) could have; (i) effect in the biodistribution of the $Na^{99m}TcO_4$ (ii) action in some organs altering the concentration of some biomarkers.

INTRODUCTION: Investigations have shown that the exposure to vibrations generated in oscillating/vibratory platform produces whole body vibration (WBV) exercises.



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Authors have reported that these exercises can increase the leg muscle force, power, rate of force development and movement velocity ^{1, 2}. Moreover, provide significant improvements in the functional capacity in severe chronic obstructive pulmonary disease ³. Significant increase in bone mineral density has been also reported ⁴.

Vibrations can be defined as an oscillatory motion. They can be generated in oscillating/vibratory platforms and transmitted, in general, by the feet to the whole body of a person ³.

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Frequency and amplitude of the sinusoidal vibration must be controlled ². Direct and indirect actions are probably related to the effects of the WBV ³ and the indirect effects might to be associated with the neuroendocrine system in different level.

The effect of the vibrations in the concentrations of some biomarkers has been investigated for various authors ^{5, 6, 7}. In other kind of experimental models, Pereira *et al.*, ⁸ have shown that, in rats, the exposure to vibration can alter the uptake of a radiopharmaceutical in stomach, bowel, kidneys, urinary bladder and prostate.

Authors have demonstrated an association between the effect of the WBV and some substances, as (i) the benefit of WBV exercise for improving physical function in postmenopausal osteoporotic women treated with alendronate ⁹ and (ii) added benefit with regard to walking, Timed up and go performance, and endurance capacity in elderly submitted to WBV training and on vitamin D supplementation ¹⁰. Naghii et al, ¹¹ have studied the effect of consumption of fatty acids and selected nutrients, along with regular WBV (10-50Hz), on cardiovascular disease (CVD) risk factors. The findings show that WBV is effective in improving health status by influencing CVD risk factors.

Natural products have been used by the human beings as food source and as medications ¹². However, the mechanism of action and the efficacy of these natural products in most cases must be validated scientifically ¹³. Due to the growth in consumption ¹⁴, facility in acquiring and still limited knowledge of biological effects on plant extracts, it is necessary further scientific research on the biological actions of these products ¹⁵.

Coriandrum sativum (Coriander) is an herbaceous plant originally from the Mediterranean and Middle Eastern regions, belonging to family *Apiaceae* ¹⁶. It is cultivated for its aromatic leaves and seeds in North Africa, Central Europe and Asia as a spice and medicine ¹⁷.

In traditional medicine, coriander is used for the treatment of diabetes, gastrointestinal complications such as dyspepsia, flatulence, diarrhea and vomiting and as an antiseptic and emmenagogue ¹⁸. It is a source of calcium (188 mg/100g), iron (3mg/100g), vitamin C (75mg/100g) and pro-vitamin A ¹⁹. Moreover, its phenolic constituents entitle the aqueous extract an antioxidant potential ²⁰. It also affects the metabolism of glucose, decreasing the glycemic level in rats ¹⁸.

Several experimental models have been used to assess the effect of the WBV ⁴, of the natural products ¹⁸ and the effect of WBV and substances ^{12, 13} and some of them use radiopharmaceuticals ⁸. Technetium-99m (^{99m}Tc), as sodium pertechnetate (Na^{99m}TcO₄), is the most widely used radionuclide in diagnostic nuclear medicine procedures in Single Photon Emission Computed Tomography (SPECT) examinations ²¹. ^{99m}Tc-radiopharmaceutical has also been used in studies to evaluate the effects of drugs ²² and plant extracts ²³.

Na^{99m}TcO₄, as a radiopharmaceutical, is distributed through the vascular and interstitial fluids and generally shows preferential uptake in the thyroid, stomach, intestinal tract, and salivary glands ²¹. Factors such as drug therapy (synthetic and natural products), radiation therapy, surgical procedures, diet conditions, and diseases can affect the biodistribution of different radiopharmaceuticals ²⁴

To our knowledge, using the information obtained in the PubMed, no previous studies have evaluated if the whole body vibration alter the effect of a *Coriandrum sativum* extract on biodistribution of the radiopharmaceutical sodium pertechnetate and on the concentration of the some biomarkers in *Wistar* rats. The aim of this study was to evaluate if the whole body vibration modify the effect of a *Coriandrum sativum* extract on the biodistribution of Na^{99m}TcO₄ and in some biomarkers in rats.

MATERIAL AND METHODS:

Animals and Ethical approach: Adult male Wistar rats (n=16) weighing between 250 and 300 g, aging from 3 to 4 months. The animals were kept under care at average temperature of 25°C, relative humidity around 55% and light/dark cycle of 12h and were fed with standard diet and water ad libitum. All experiments were conducted following the standards of the Comitê de Ética Para o Uso de

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Animais Exprimentais (CEUA), Instituto de Biologia Roberto Alcantara Gomes that was approved with the registration number CEUA/041/2011.

Characteristics of the oscillating platform: The platform used in the experiment is an oscillating system (Novaplate fitness evolution, DAF, *Produtos Hospitalares Ltda, São Paulo*) with reciprocating vertical displacements on the left and right side of a fulcrum. It is a side-alternating vibration device working as a teeterboard (28cm x 58cm) with amplitude of 0 (zero) mm in the center of the platform up to the maximum in the edge that was 7.07 mm.

Preparation of the extract of Coriander: A commercial dry extract of Coriander (*Coriandrum sativum*) was used (lot 0046, validity up to July 2014, *Distribuidora de Cereais Crowne Ltda, Rio de Janeiro*). This natural product was chosen because it is also used a medicinal plant. To prepare the extract, 80 mg of *Coriandrum sativum* were added 10 mL of 0.9% NaCl solution. Then, the preparation was vortexed for 1 minute, centrifuged (clinical centrifuge, 15000 rpm, 15 minutes) and the supernatant was considered to be at a concentration of 8 mg/mL.

Experimental procedures: The *Wistar* rats (n=16) were divided in four groups. The animals of the control group (CON) received by gavage ²⁵ 1.0 mL of 0.9%NaCl solution (saline). The animals of the group treated with 1.0 mL coriander 8g/mL (COR) received the extract by the same via. The rats that were submitted to the vibration generated in the platform (PLA) also received 1.0 mL of saline. Animals of the group (COR + PLA) received 1.0 mL coriander 8g/mL and were submitted to vibration generated in the platform.

The animals received saline (group CON) or coriander extract (groups COR and COR + PLA) every day during ten consecutive days.

The animals of the groups PLA and COR + PLA were submitted every day during ten consecutive days to vibrations generated in the platform. The frequency used was 12 Hz and the work time was 3 min.

This frequency has also used by Turner *et al.*, 26 . The animals were put in a man-made acrylic base fixed in the teeterboard of the platform with tape, as it is shown in **Figure 1**.



FIG. 1: WISTAR RATS ON THE PLATFORM

Every day the animals of CON and COR groups were put close the platform (about 30 cm) that was turn on. However, the animals did not have a direct contact with the platform.

In this investigation was followed a similar total time per day reported by Pawlak *et al.*, ⁷ in the treatment of the rats in the platform.

Administration of the radiopharmaceuticals and obtainment of blood samples: At the end of 10 days, the animals were anesthetized with sodium thiopental. Just after the animals were under the effect of the anesthesia, the radiopharmaceutical Na^{99m}TcO₄ (3.7 MBq) was administrated via ocular plexus. After 10 min, sample of blood obtained from by cardiac puncture was used for biochemical analysis. Following, the animals were sacrificed, the organs isolates, the radioactivity determined in a well counter, and the percentages of radioactivity per gram (% ATI/g) in the organs were calculated as reported elsewhere ⁸.

The concentrations of selected biomarkers (glucose, creatinine, cholesterol, triglyceride, HDL, alkaline phosphatase, bilirubin, amylase, lipase, CK, calcium, magnesium, total protein and albumin) were then measured in a clinical laboratory of the *Universidade do Estado do Rio de Janeiro*. The determinations were performed in automated equipment (COBAS INTEGRA 400 plus, Roche, Basel, Switzerland).

Statistical analysis: An ANOVA (Kruskal-Wallis) test was used following the post-test Student-Newman-Keuls was done for the statistical analysis of the results. Data are presents as mean \pm standard deviation (\pm SD). Statistical significance was accept at p<0.05.

RESULTS: Table 1 shows the %ATI/g of the Na^{99m}TcO₄ in the various organs isolated from the animals submitted to different treatments.

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TABLE 1: %ATI/G IN ORGANS ISOLATED FROM THE ANIMALS SUBMITTED TO DIFFERENT TREATMENTS

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ORGANS	CON	COR	PLAT	COR+PLAT	p
Thyroid	4.17±2.38	5.69 ± 2.38	4.79 ± 1.50	5.37±0.58	0.5663
Stomach	2.35 ± 0.77	2.65 ± 1.26	2.33 ± 0.70	2.57 ± 0.73	0.9025
Bowel	0.61 ± 0.23	0.68 ± 0.21	1.00 ± 0.82	0.82 ± 0.67	0.8718
Kidney	0.43 ± 0.10	0.50 ± 0.06	0.51 ± 0.11	0.56 ± 0.04	0.4233
Liver	0.43 ± 0.09	0.59 ± 0.09	0.61 ± 0.12	0.59 ± 0.30	0.2143
Pancreas	0.21 ± 0.12	0.39 ± 0.16	0.31 ± 0.14	0.50 ± 0.23	0.2483
Brain	0.02 ± 0.01	0.02 ± 0.00	0.016 ± 0.00	0.017 ± 0.00	0.1109
Bone	0.08 ± 0.07	0.22 ± 0.03	0.17 ± 0.12	0.54 ± 0.07	0.1339
Lung	0.52 ± 0.09	0.67 ± 0.19	0.87 ± 0.22	0.92 ± 0.39	0.1160
Heart	0.20 ± 0.06	0.21 ± 0.04	0.21 ± 0.04	0.23 ± 0.05	0.9269
Spleen *	0.22 ± 0.02	0.27 ± 0.04	0.31 ± 0.01	0.35 ± 0.02	0.0101*
Muscle	0.07 ± 0.02	0.15 ± 0.02	0.11 ± 0.03	0.15 ± 0.05	0.0559
Blood	0.91 ± 0.42	1.03 ± 0.14	0.97±0.17	0.90 ± 0.21	0.8509

CON- crontol group; COR- group treated with coriander, PLAT- group submitted to vibration generated in platform, COR+PLAT- group treated with coriander and submitted to vibration

It is possible to verify that only in spleen was found a significant (p<0.05) alteration, in comparison with the CON group, the uptake of the radiopharmaceutical in the animals submitted to the vibration (PLA group) and vibration and treated with coriander (COR + PLA group). Another

significant (p<0.05) alteration was found in the comparison between the COR group and (COR + PLA group). **Table 2** shows the concentration of some biomarkers that was determined in the animals submitted to different treatments.

TABLE 2: CONCENTRATION OF SOME BIOMARKERS DETERMINED IN ANIMALS SUBMITTED TO DIFFERENT TREATMENTS

	CON	COR	PLAT	COR+PLAT	p
Glucose (mmol/L)	8.03±0.13	8.22±0.49	7.49 ± 0.52	7.71±0.70	0.4803
Creatinine(mg/dL)	0.35 ± 0.05	0.30 ± 0.00	0.32 ± 0.05	0.30 ± 0.00	0.2376
Cholesterol (mg/dL)	70.50 ± 9.03	56.50±7.59	60.50±9.29	61.50 ± 4.20	0.0457*
Triglyceride (mg/dL)	65.33±6.65	28.75 ± 14.17	36.00 ± 3.00	32.00±22.49	0.0325*
HDL (mg/dL)	60.50±8.18	50.50 ± 4.65	52.75 ± 6.39	50.5 ± 4.20	0.2148
Alkaline Phosphatase (U/L)	109.75±27.15	187±12.56	155 ± 38.34	141.25 ± 25.87	0.0412*
Bilirubin (mg/dL)	0.06 ± 0.005	0.04 ± 0.005	0.04 ± 0.012	0.03 ± 0.012	0.0291*
Amilase (U/L)	2763.25±155.04	2899.75±428.53	2754±230.23	2546.75±556.67	0.5801
Lípase (U/L)	5.37 ± 0.34	5.27 ± 0.15	5.37 ± 0.35	5.20 ± 0.46	0.8455
CK (U/L)	427±84.85	1332.667±32.12	520.66±172.70	802.25±380.19	0.0165*
Calcium (mg/dL)	11.22±0.66	11.425±0.37	10.45±0.36	10.75 ± 0.98	0.1134
Magnesium (mg/dL)	2.15±0.17	2.3 ± 0.42	2.62 ± 0.28	2.2 ± 0.18	0.2325
Total Protein(mg/dL)	5.82 ± 0.30	5.47 ± 0.12	5.72 ± 0.17	5.65 ± 0.25	0.2152
Albumin (mg/dL)	3.77±0.26	3.57±0.15	3.77±0.12	3.50±0.16	0.118

CON- control group; COR- group treated with coriander, PLAT- group submitted to vibration generated in platform, COR+PLAT- group treated with coriander and submitted to vibration.

Significant (p<0.05) alterations were found in concentrations of the cholesterol (CON compared with COR and between CON and PLAT), triglyceride (CON compared with the groups COR, PLAT and COR+PLAT), alkaline phosphatase (CON compared with COR), bilirubin and CK (CON and COR, and COR and PLAT).

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DISCUSSION: Studies involving the evaluation of the association between the effect of the WBV and some substances ^{9, 10, 11} have stimulated our investigation. In particular, Naghii *et al*, ¹¹ has evaluated the association of WBV (10-50Hz) with some natural medicinal products (canola oil, sunflower oil, mix of sunflower oil and canola oil and coconut oil). In our work, the consequences of the treatments with whole body vibration and a medicinal product (*Coriandrum sativum*) extract on the biodistribution of the radiopharmaceutical ^{99m}Tc-sodium pertechnetate and some biomarkers in *Wistar* rats were assessed.

The findings reported in this investigation permit to verify the effect of the proposed protocol using vibration with the frequency of 12 Hz and the extract of coriander in organs, as well as in the concentration of some biomarkers related to the metabolism.

The determination of the uptake of the radiopharmaceutical sodium pertechnetate in different organs (Table 1) permits to verify that extract of coriander alone was not capable in interfering in the biodistribution the radiopharmaceutical. However, the treatment of the animals with vibration generated in the platform alter significantly (p<0.05) the fixation of the sodium pertechnetate in the spleen. Some authors have supposed an effect in organs of the digestory system related to the coriander, as gastrointestinal complications such as dyspepsia, flatulence, diarrhea and vomiting and an action in the metabolism of glucose ¹⁸.

The effect in the spleen is (Table 1) only in the association with the WBV. A very interesting found is that the association between the coriander and the vibration were capable in increasing the uptake of the radiopharmaceutical. Pereira *et al.*, 8 have shown that, in rats, the exposure to vibration with 20 Hz can alter the uptake of a radiopharmaceutical in stomach, bowel, kidneys, urinary bladder and prostate. Miyazaki, ²⁷ has evaluated the electrogastrography (EGG) in healthy male volunteers' exposure to vibration of 4, 8 and 16 Hz. This author has observed that only the vibration of 4 and 8 Hz have decreased the amplitude of the EGG.

Putting together these findings is interesting suggest the biological effects can be dependent on the frequency of the vibration used in the WBV.

The determination of the effect of the treatments in the concentration of the biomarkers (Table 2) has shown interesting findings. Pettersson *et al* ²⁸ showed that heavy weight training in healthy men affected liver functions. High levels of serum CK have been associated with swelling and muscle soreness experienced in (untrained) athletes ²⁹. Gojanovic *et al* ³⁰ found that five participants (25%) who took part in a training program showed a significant increase in post-exercise CK levels (> double baseline concentrations).

Naghii *et al* ⁶ have reported in male rats submitted to vibrations with frequencies of 10-50 Hz significant differences in plasma levels of CK, and plasma CK levels were significantly higher in the vibration group compared with the controls. Our findings (Table 1) showed that vibration of 12 Hz alone did not alter the concentration of CK, but the association with the coriander extract increased the concentration of this biomarker, as well as, the extract of the medicinal plant alone. These effects associated with the coriander could be related to the important presence of some substances in the coriander extract, as calcium, iron, vitamin C and pro-vitamin A ¹⁹.

Although a significant alteration in the concentration of the bilirubin was found in the COR group and in the COR + PLAT group in comparison with the CON group, we are considering as a no important alteration (small differences in the concentration among the groups), due to some other biomarker related to the liver functions ³¹ was not altered, as the albumin. The concentration of the alkaline phosphatase was only altered in the group COR in comparison with the control group.

Naghii $et\ al\ ^6$ have determined the plasma lipid concentrations (total cholesterol, LDL and HDL) in rats submitted to vibrations in the frequencies of 10-50 Hz and they did not found alteration in the concentrations of these biomarkers. However, we have found a significant alteration in the concentration of the cholesterol in the group of

animals submitted to the vibration of 12 Hz with a different protocol compared with Naghii *et al.*, ⁶. Moreover, the extract of the coriander has also decreased the concentration of the serum cholesterol and this fact could be associated with the as gastrointestinal effects described ¹⁸.

Goto and Takamatsu ⁵, have already reported changes in the fatty acid concentrations due to the action of the vibration (PLAT group) generated in the platform and the results present in the Table 2 are in agreement with this finding. Moreover, the extract of coriander (COR group) and the association of this extract (PLAT + COR group) with the vibration have also effect in decreasing the concentration of triglycerides.

CONCLUSION: Putting together all the findings reported in this investigation, the results indicated that the treatment with the association of an extract of coriander and vibration generated in platform with the frequency of 12 Hz could have (i) effect in the spleen, as observed by the alteration in the fixation of the radiopharmaceutical in this organ and (ii) action in some organs altering the concentration of some biomarkers.

COMPETING INTERESTS: The authors declare that they have no competing interests.

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