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**Review Article**

# *In Vitro* and *In Vivo* Studies of the Biological Effects of Bioceramic (a Material of Emitting High Performance Far-Infrared Ray) Irradiation

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## Abstract

**Bioceramic is a material that emits high performance far-infrared ray, and possess physical, chemical and biological characteristics on irradiation of water, particularly to in reducing the size of water clusters, weakening of the hydrogen bonds of water molecules and other effects on physical and chemical properties of water. In this review paper, we summarized the *in vivo* and *in vitro* biological effects of Biocermaic, and included previous published data on nitric oxide, calmodulin induction on cells, effects of Bioceramic on intracellular heat shock protein and intracellular nitric oxide contents of melanoma cells, antioxidant effects of Bioceramic on cells and plants under $H_2O_2$-mediated oxidative stress, effects on anti-oxidative stress of myoblast cells and on preventing fatigue of amphibian skeletal muscle during exercise, anti-inflammatory and pain relief mechanism, effects on the chondrosarcoma cell line with prostaglandin E2 production, effects on the rabbit with inflammatory arthritis by injection of lipopolysaccharides under monitoring by positron emission tomography scan, effects on psychological stress-conditioned elevated heart rate, blood pressure and oxidative stress-suppressed cardiac contractility, and protective effects of non-ionized radiation against oxidative stress on human breast epithelial cell. We anticipate that the present work will benefit medical applications.**

**Key Words: anti-inflammation, antioxidant, Bioceramic, calmodulin, far infrared ray, heat shock protein, muscle fatigue, nitric oxide**

## Introduction

Far infrared ray is non-ionizing electromagnetic radiation with wavelengths of 4-16 μm (23). Bioceramic, a material that emits far-infrared ray, is a source of high performance far infrared ray that exhibits mainly non-thermal effects at room temperature. Physical, chemical and biological effects of Bioceramic irradiation on water, including reducing the size of water clusters, weakening of the hydrogen bonds of water molecules, and other effects on physical and chemistry properties of water have been investigated (7, 13). Our previous studies (1, 3-23) have also shown that Bioceramic treatment promotes microcirculation in patients (23) and up-regulation of calcium-dependent nitric oxide (NO) and calmodulin (CaM)

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in cell lines (9, 14). We further demonstrated that Bioceramic treatment on cells promoted NO enhancement through calcium-dependent nitric oxide synthetase (NOS) (9, 14). Bioceramic treatment demonstrated antioxidant effects by increasing hydrogen peroxide ($H_2O_2$) scavenging processes in RAW264.7 murine macrophages (15), MC3T3-E1 murine calvaria-derived osteoblast-like cells (5), NIH3T3 fibroblasts (17) and C2C12 murine myoblasts (10) and other cells and animal experimental effects. Bioceramic may contribute to physical, chemical and biological properties on different testing specimens, such as water, volatile materials, weak acids and living cells, as well as enhancement of transdermal delivery of different drugs (20). Many of our previous publications (1, 3-23) were cited in reviews and research articles, including researchers of Massachusetts Institute of Technology, Harvard Medical School, Massachusetts General Hospital (24) and others (2). In this review, we present an integrated view of our previous publications on studies on biological effects of Bioceramic irradiation.

*The Bioceramic Material*

The Bioceramic powder used in this study, obtained from the Bioenergy laboratory, Bioenergy Development Ltd, Taoyuan, Taiwan, ROC, was composed of micro-sized particles produced from several ingredients mainly of different elemental components (1, 3-23). The average emissivity of the ceramic powder was 0.98 at wavelengths of 6-14 μm (determined by a CI SR5000 spectro-radiometer), which represents an extremely high ratio of Bioceramic intensity (Fig. 1). Many physical, chemical and biological effects can be induced with this ceramic powder at room temperature without the necessity of direct contact (1, 3-23).

*NO Induction by Bioceramic on MCF-70 Cells*

NO is a compound that plays different roles in the body, including: [1] vasodilator; [2] controlling blood flow to tissues; [3] regulating the binding and release of oxygen to hemoglobin; [4] controlling the supply of oxygen to mitochondria; [5] killing parasitic organisms, virus-infected cells and tumor cells; [6] stimulating the production of new mitochondria (9). We investigated the influence of Bioceramic in generating NO in cells. MCF-7 breast cancer cells were treated with Bioceramic irradiation, and the inducible NO concentrations were measured using the DAF-FM diacetate technique by using flow cytometric measurements. Mean fluorescence intensities of different cell groups showed progressive and cumulative increases in NO in the Bioceramic groups with significant differences from the control groups. Significant inductions of NO synthesis in cells were observed both during and after Bioceramic irradiation (4, 9).

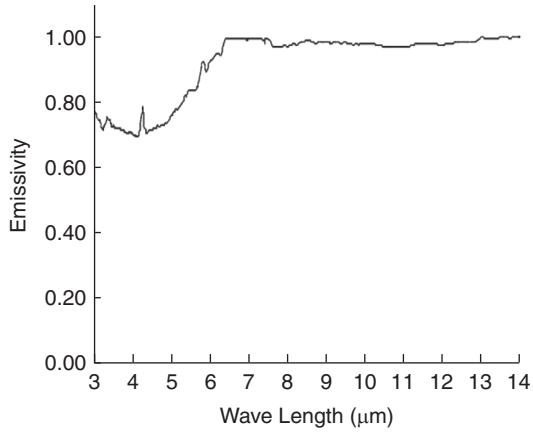


Fig. 1. The range of wavelength represent far infrared ray is from 8-14 μm, and the average emissivity of the ceramic powder is over 0.90.

*CaM- and Calcium-Dependent NO in Macrophage Cells RAW264.7 Induced by Bioceramic*

CaM is a calcium-binding messenger protein expressed in all eukaryotic cells. CaM transduces calcium signals by binding calcium ions and then modifying its interactions with various target proteins, and mediates processes of inflammation, metabolism, apoptosis, smooth muscle contraction, intracellular movement, short- and long-term memory and the immune response. We investigated the effects of Bioceramic on the expression of CaM in and NO production by RAW264.7 macrophages by Western blotting technique. Results indicated a significant increase in CaM protein in Bioceramic-treated RAW 264.7 macrophages with or without the addition of lipopolysaccharide (LPS). In addition, the amount of NO was slightly higher but increased significantly in Bioceramic plus LPS-treated RAW 264.7 macrophages. Data of the study provide information on immunomodulatory properties of Bioceramic through increasing CaM protein and NO production in RAW 264.7 macrophages (14). In mammals, NO is mediated by the calcium-CaM-controlled endothelial nitric oxide synthetase (eNOS) and neuronal nitric oxide synthetase (nNOS). They are also known as constitutive nitric oxide synthetase (cNOS) and calcium-dependent NOS. On the other hand, inducible nitric oxide synthetase (iNOS) is involved in immune response, and produces large amount of NO as an immune defense mechanism. Macrophages play critical roles in both the innate immune response to pathogens and normal clearance of apoptotic cells and cell debris. The phagocytic process of macrophages requires an interaction between the calcium-signaling protein, CaM and binding

partners, including iNOS, which in turn produces NO to enhance the immunomodulatory effect. Although there was an equivocal effect of an increase in the level of NO by macrophage cells in the Bioceramic group, the effect seemed to be more prominent when a second stimulation with LPS was applied. But if these two results are compared, it seems that CaM induction by Bioceramic was stronger than NO induction by Bioceramic in RAW 264.7 cells. Under normal and basal conditions, the activity of iNOS is very low. During inflammation, the amount of NO produced by iNOS in macrophages may be 1,000-fold greater than that produced by cNOS. It is believed that cNOS and iNOS differ in their $Ca^{2+}$/CaM dependency. cNOS is regulated by the reversible binding of CaM through changes in the intracellular $Ca^{2+}$ concentration, whereas iNOS is expressed by permanently bound CaM and remains active in the absence of free $Ca^{2+}$. NO production by macrophages has long been investigated as a result of iNOS activation. Nevertheless, we found that a rapid increase in the level of CaM resulted in a response by RAW 264.7 macrophages by Bioceramic irrespective of exposure or not to LPS. On the other hand, iNOS did not respond in such a quick manner in the beginning. From this result, we deduced that the Bioceramic effects on CaM occurred more directly, and perhaps the CaM response occurred prior to that of NO induction in RAW 264.7 cells. It is known that calcium-dependent nitric oxide cNOS is regulated by CaM through changes in the intracellular $Ca^{2+}$ ion concentration, and that iNOS is expressed by permanently bound CaM and remains active in the absence of free $Ca^{2+}$ ions. Bioceramic-induced NO is continually being produced by cNOS, and the activity of cNOS is CaM-dependent, and thus calcium-dependent. Hence, NO enhanced by Bioceramic is cNOS-dependent and not iNOS-dependent, as is described in the additional experiment described below (4, 9, 14).

*Effects of Bioceramic on Intracellular Heat Shock Protein (HSP)70 and Intracellular NO Contents of Melanoma Cells*

The biological effects of specific wavelengths, the so-called "far-infrared radiation" produced from Bioceramic, on whole organisms are not yet well understood. In this study, we investigated the biological effects of Bioceramic on murine melanoma B16-F10 cells at body temperature. Bioceramic irradiation treatment for 48 h resulted in an 11.8% decrease in the proliferation of melanoma cells relative to the control. On the other hand, incubation of cells with Bioceramic for 48 h resulted in 56.9% and 15.7% significant decreases in the intracellular heat shock protein (HSP-70) and intracellular iNO contents, respectively. Furthermore, Bioceramic treatment induced 6.4% and 12.3%

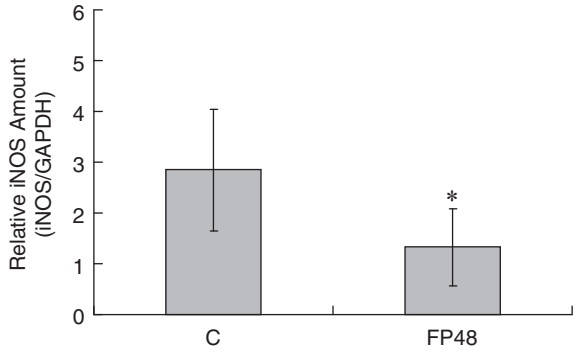


Fig. 2. Comparison of inducible nitric oxide synthase between the control (group FP48) and cFIR (group FP48) groups. Expression values are the mean and standard deviation, and the difference between groups was tested using the Wilcoxon test.

increases in intracellular reactive oxygen species (ROS) stained by 5-(and 6)-carboxy-2',7'-dichlorodihydrofluorescein diacetate and dihydrorhodamine 123, respectively. Since malignant melanomas are known to have high HSP-70 expression levels and iNO activities, the suppressive effects of Bioceramic on HSP-70 and NO may warrant future interests in antitumor applications. Analysis of iNOS expression in B16-F10 cells subjected to a 48 h interval with or without cFIR (ceramic far infrared ray) treatment was performed by Western blotting. The normalized mean production of iNOS protein (iNOS/GAPDH) in group C (control) and group FP48 (Bioceramic irradiated for 48 h) were $2.85 \pm 1.19$ and $1.33 \pm 0.75$, respectively (Fig. 2). This result may reflect the ability of Bioceramic to suppress iNOS expression in B16-F10 cells. Bioceramic is a somatothermal process without an additional thermal effect on murine melanoma cells. Bioceramic is capable of suppressing the proliferation of B16-F10 cells and inhibiting intracellular NO and HSP-70 production. Treatment with Bioceramic induced intracellular reactive oxygen species (ROS) production but did not significantly affect cell apoptosis, leading us to speculate interference with the cell cycle, such as cell growth arrest. We deduced that the melanoma inhibitory effect may be a consequence of or share a common pathway with the decreased intracellular HSP-70 and NO. Further investigations into the basic biomolecular and physiological mechanisms occurring in melanoma cells following Bioceramic treatment will help future therapeutic applications of Bioceramic (4).

*Antioxidant Effects of Bioceramic on Animal Cells and Plants under $H_2O_2$-Mediated Oxidative Stress*

Bioceramic has several proven effects on the human body that are generally considered to be bio-

logically beneficial. We determined the effects of Bioceramic on $H_2O_2$-scavenging activity, which was directly increased by 10.26% after Bioceramic application. Even in the indirect use of Bioceramic on carrot extract, Bioceramic still contributed to a 5.48% increase in $H_2O_2$-scavenging activities. We further proved that additional Bioceramic treatment resulted in 23.02% and 18.77% increases in the viability of osteoblast cells when treated with 200 and 800 μM $H_2O_2$, respectively, and 25.67% and 47.16% viability increases of fibroblast cells in the 25 and 50 μM $H_2O_2$, respectively. Bioceramic treatment also delayed senescence of detached Railway Beggarticks leaves in 10, 100, and 1,000 μM $H_2O_2$ solution. By reviewing past articles related to the effects of oxidative stress from metabolically produced $H_2O_2$, we discussed possible benefits of Bioceramic for plants and animals. In addition, the leaves in Bioceramic groups showed delay in senescence by observations of the leaf-yellowing process. These results reflect that there was less chlorophyll breakdown of leaves in Bioceramic groups than the control groups (17). A study was aimed to explore the effects of Bioceramic on RAW 264.7 cells by determining the scavenging activity of $H_2O_2$, cell viability and changes in cytochrome *c* levels and the $NADP^+$/NADPH ratios. The results showed that the $H_2O_2$-scavenging activity directly increased by 10.26% after Bioceramic application. Additional Bioceramic treatment resulted in increased viability of murine macrophages with different concentrations of $H_2O_2$. Bioceramic significantly inhibited intracellular peroxide levels and LPS-induced peroxide production by macrophages. The increased ratio of hypodiploid cells elicited by $H_2O_2$ was significantly reduced by Bioceramic. The effects of Bioceramic on $H_2O_2$ toxicity were determined by measuring intracellular changes in cytochrome *c* levels and the ratio of $NADP^+$/NADPH, and results showed that Bioceramic may block ROS-mediated cytotoxicity. It may thus be worthwhile for applications of Bioceramic for its antioxidant, anti-aging, immunity-boosting and other related health-promoting effects. However, to better elucidate the precise effects of Bioceramic on living systems, it is important that future research should develop an *in vivo* experimental model. We believe that these results justify further work to develop a more mature explanation of the biomolecular mechanisms of Bioceramic with regard to mammalian cells as showed in Fig. 3 (15).

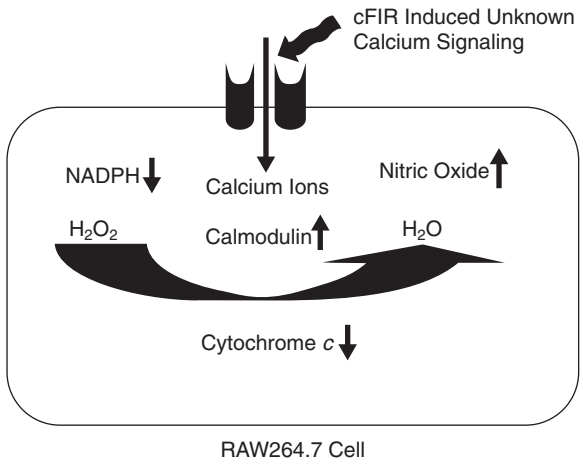


Fig. 3. A possible pathway through which Bioceramic achieves its antioxidant effects.

*Effects of Bioceramic on Exercise Physiology by Anti-Oxidative Stress of Myoblast Cells and by Preventing Fatigue of Amphibian Skeletal Muscle during Exercise*

A study was conducted to assess the potential for Bioceramic to improve exercise performance at room temperature. We designed the experiments with murine myoblast C2C12 cells to study the effect of Bioceramic irradiation on cell viability and lactate dehydrogenase release under $H_2O_2$-mediated oxidative stress, and also evaluated intracellular levels of NO and CaM. Electro-stimulation of amphibian skeletal muscle was also used (10). As shown in Fig. 4, the stimulator was used to obtain maximum contraction power by adjusting the power supply. The stimulator stimulated the muscle with continuous pulses at intervals of five mini-seconds for periods of one second. The purpose of this experiment was to stimulate the muscle continually for a long period of time, and record the loading contraction force (in grams) and time until onset of muscle fatigue. Before electro-stimulation of isometric contractions, the right and left muscles from the same frog were randomized to matching and fully surrounded either by Bioceramic silicon rubber or ordinary silicon rubber bracelets, but without direct contact (Fig. 4). The contraction force was recorded during continuous electro-stimulation until both muscles were fatigued. Comparison of the mean contraction force (mean time of contraction before complete fatigue) between the Bioceramic and control groups was performed. A series of experiments with pairs of right and left gastrocnemius muscles were performed consecutively according to these procedures. In a series of electro-stimulation experiments, though both of the muscles were from the same amphibian animal, they showed different contraction forces at the beginning. Even though the initial contractive loading of the Bioceramic group was weaker than the control group, the Bioceramic samples continued contracting longer than those of the control group. In addition, there was a significant difference ($P < 0.05$) between the two groups

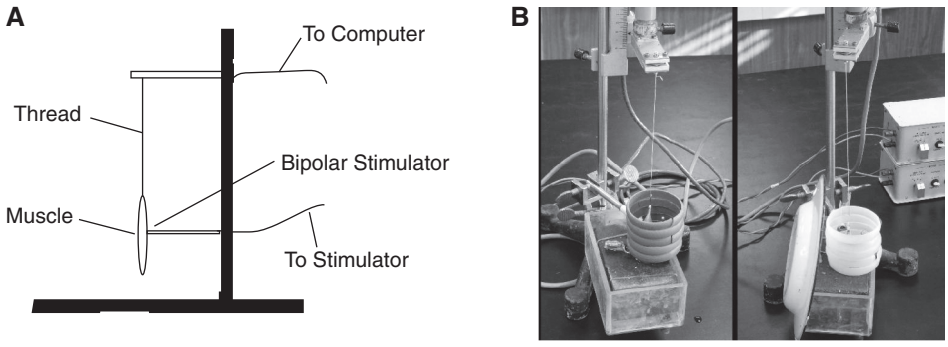


Fig. 4. Schematic view (A) and the actual view (B) of the muscle stimulation experiment. During the electro-stimulation of amphibian skeletal muscles isolates from the same individual frog, the muscles were matched using Bioceramic bracelets (left, Bioceramic group) and control bracelets (right, control group).

in the mean contraction load (mean duration of contraction before complete fatigue). Results indicate that Bioceramic bracelets can reduce fatigue in amphibian muscles (Fig. 5).

*Measurement of pH Changes after Fatigue from Electro-Stimulated Isometric Contractions by Bioceramic*

Pre-test of the muscles by measuring pH values on the same frog included (a) before electro-stimulation, (b) after 20 min of electro-stimulation of the control muscle and (c) after 20 min of electro-stimulation of the cFIR- irradiated muscle. After consecutive electro-stimulation of contractions, a number of two right and left fatigued muscles in pairs of the Bioceramic and control groups were then frozen in liquid nitrogen. The muscle samples were homogenized in deionized water and pH values was subsequently determined. After pH value data was obtained, the ratios between the contraction force and final pH value of Bioceramic and the control groups were compared. This experiment showed that metabolic acid accumulation after electro-stimulation caused a measurable pH value decrease in muscles, and the presence of Bioceramic could normalize acidification following muscle contractions. In this pilot study, we found that Bioceramic may reduce muscular fatigue and normalized acidification of contracted muscles. The beneficial effects of Bioceramic for delaying the onset of fatigue might originate from its antioxidant properties preventing metabolic acidosis of muscular fiber. The results showed that Bioceramic strengthened C2C12 under oxidative stress and delayed onset of fatigue induced by muscle contractions (10).

In Vitro *Study of Possible Anti-Inflammatory and Pain Relief Mechanism by Bioceramic*

Under the effects of Bioceramic, effective doses of LPS was added to induce acute episodes of inflammation to murine macrophage RAW264.7 and human chondrosarcoma SW1353 cells. Inducible NO synthetase (iNOS), cyclo-oxygenase-2 (COX-2) and prostaglandin E2 (PGE2) levels in the cell lines were determined. We showed that, Bioceramic treatment, significantly inhibited COX-2, PGE2, and probably iNOS in the cell models of LPS-mediated inflammation (Fig. 6). Bioceramic may be an alternative method for palliative pain control to reduce chemical drug dependence for the protection of renal functions in the population with chronic pain diseases (16).

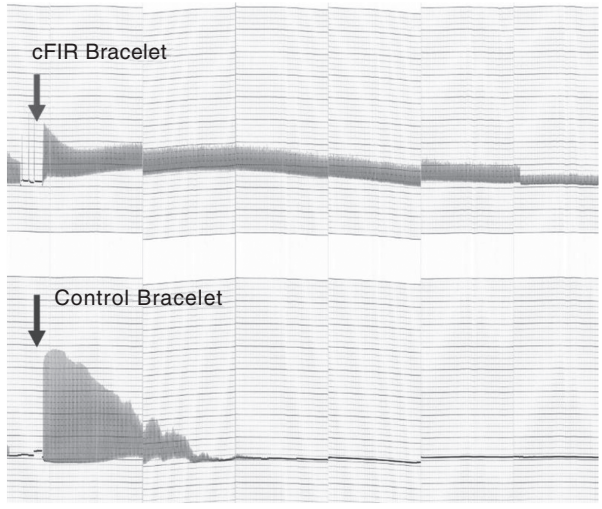


Fig. 5. The gastrocnemius muscle contraction record chart. Bioceramic group prolonged the fatigue process of the muscle, even though the initial contraction force was weaker than the control group.

*Effects of Bioceramic on a Chondrosarcoma Cell Line with Prostaglandin E2 (PGE2) Production*

To investigate the effect of Bioceramic on PGE2 production, PGE2 accumulation in the culture media was measured after 48 h of 20 ng/ml LPS induction

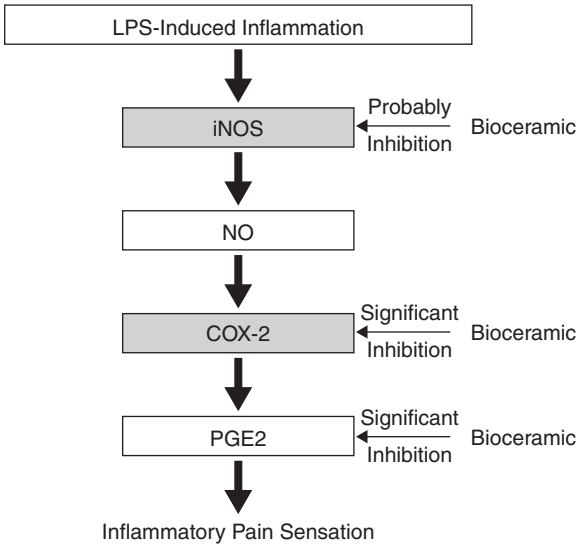


Fig. 6. Proposed model of Biocearmic interaction with the signaling pathways of LPS- induced inflammation through iNOS, COX-2 and PGE2 to produce inflammatory pain sensation. Bioceramic exhibited the significant inhibitory effects on COX-2 and PGE2, and probably on iNOS.

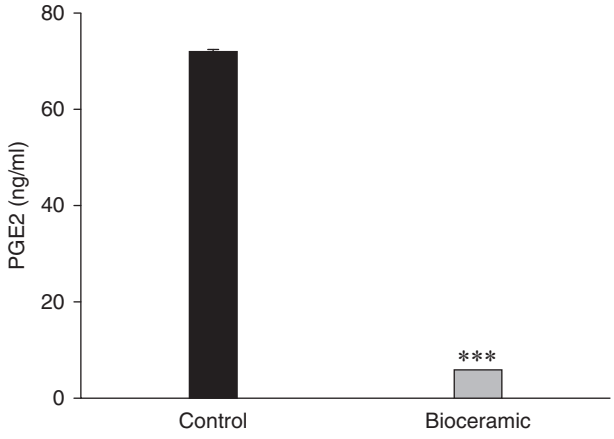


Fig. 7. Comparison of LPS-induced PGE2 of SW1353 cell line in the control and experimental groups (n = 5). ***$P <$ 0.0001, significantly different compared with the control group.

with or without the placement of the Bioceramic material beneath the cell medium discs. In the cultured disc of the experimental group, treatment of LPS caused production of lower amounts of PGE2 than the LPS-treated control group (Fig. 7). This result reflects a significant suppression of the LPS-induced PGE2 of cells by the Bioceramic material. Bioceramic was previously shown to produce an anti-inflammatory effecton joints by reversing LPS-induced arthritis in ananimal model and inhibiting PGE2 in a cell model (16).

*Effects of Bioceramic on the Rabbit Model of Arthritis by Injection of LPS and Monitoring under Positron Emission Tomography (PET) Scan*

We studied possible activities of Bioceramic under these conditions using animal and cell models. Rabbits received intra-articular injections of LPS to induce inflammation that mimics rheumatic arthritis. Fluoro-18-fluorodeoxyglucose (FDG) isotopes were then intravenously injected for positron emission tomography (PET) scan examinations at 16 h and on the 7th day after the LPS injection. We examined and compared the Bioceramic and control groups to see if Bioceramic was capable of relieving inflammation in the joints by subtracting the final and initial uptake amount of FDG (max SUV). We studied the effects in PGE2 inhibition on the SW1353 human chondrosarcoma cell line, and the effects on the murine osteoblast MC3T3-E1 cell line under oxidative stress. All the subtractions between final and initial uptakes of FDG in the left knee joints of the rabbits after LPS injection indicated larger decreases in the Bioceramic group than in the control group. These anti-arthritic or inflammatory effects were also demonstrated by the PGE2 inhibition of the SW1353 cells. We further showed that Bioceramic treatment of the MC3T3-E1 cells resulted in increased viability of osteoblast cells challenged with hydrogen peroxide toxicity, and increased alkaline phosphatase activity and the total protein production of MC3T3-E1 cells under oxidative stress. Since LPS-induced arthritis is an experimental model that mimics rheumatic or arthritis, the potential therapeutic effects of Bioceramic on arthropathy merit further discussion. Bioceramic may contribute to relieving inflammatory arthritis and maintaining bone health (5).

*PET Scan Study on Knees of Rabbits with LPS Injection under Bioceramic*

The knees of rabbits of both control and Bioceramic groups were evaluated sequentially by Micro-PET system at 16 h and on the 7th day after LPS injection. Six knees with inflammatory arthritis were examined. Figs. 8A, 8B and 8C present three standard views of typical PET image volume taken on the seventh day after LPS injection by coronal, axial and sagittal views of the knees and joints of the control and Bioceramic group. Brighter and reddish areas indicate higher radioactivity, while a yellow-greenish color represents lesser degrees of radioactivity. FDG uptake was assessed in the most metabolically active portions of both knees of each rabbit. The PET scan images for the two groups showed that two out of three amongst the control group rabbits with their LPS-induced knee joints were found to show further increase

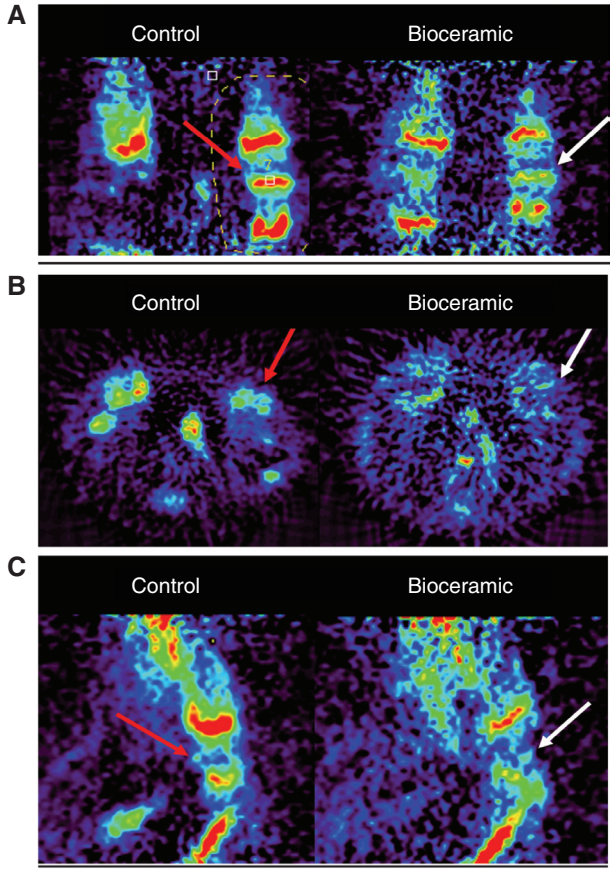


Fig. 8. Representative images of PET scan on experimental rabbits, which showed the comparison of the control [left figures, with red arrows, in coronal (A), axial (B) and sagital (C) views]; and Bioceramic group [right figures, with white arrows, in coronal (A), axial (B) and sagital (C) views], after 7 days of LPS intra-articular injection of left knees.

FDG uptake. The result was reflecting inflammation exacerbate from 16 h to 7th day. On the contrary, every LPS-injected knee in the Bioceramic-treated group exhibited significant relief of arthritis. The statistical relationship between the control and Bioceramic groups using mean of max SUVs on the 7th day and mean of the subtraction values (max SUV) by 7th day to 16 h were obtained. The *P*-values were smaller than 0.05 and 0.01 respectively, which were statistically significant. These results indicate that the Bioceramic group recovered faster from inflammatory arthritis after seven days of intra-articular LPS injections than the control group (5).

*Effects of Bioceramic on Psychological Stress-Conditioned Elevated Heart Rate, Blood Pressureand Oxidative Stress-Suppressed Cardiac Contractility*

The effects of Bioceramic on the *in vivo* cardiovascular hemodynamic parameters of rats were studied

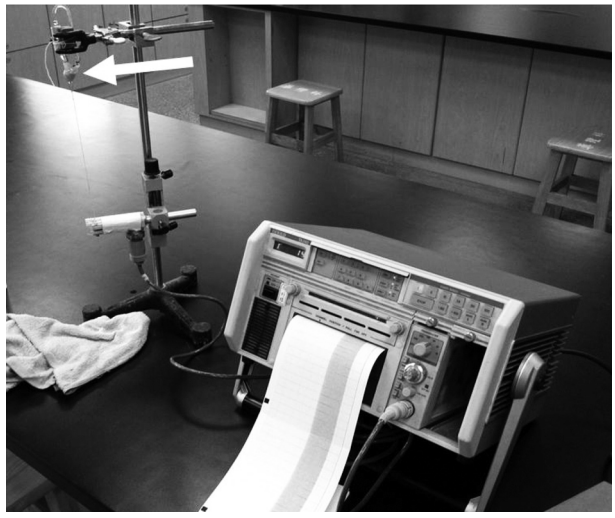

Fig. 9. Isolated beating frog heart (white arrow) connected to a contractile force recording system.

by monitoring their heart rates, systolic blood pressure, mean blood pressure and diastolic blood pressure. We assayed the Bioceramic effects on the heart rate in an isolated frog heart with and without adrenaline stimulation, and on cardiac contractility under oxidative stress. Bioceramic caused significant decreases in the heart rate and systolic and mean blood pressure in the stress-conditioned heart-rate rat models ($P < 0.05$), as well as in the experimental models of an isolated frog heart with and without adrenaline stimulation ($P < 0.05$), and normalized cardiac contractility under oxidative stress ($P < 0.05$). Bioceramic normalized the effects of psychological stress and oxidative stress conditions (Fig. 9). Bioceramic have beneficial effects on the heart during oxidative stress, by suppressing contractility and potentially ameliorating long-term oxidative stress, thus, reducing the likelihood of cardiac arrest and ischemic myocardial injury. Bioceramic was proven to normalize psychological stress-conditioned elevated heart rate and blood pressure, as well as oxidative stress-suppressed cardiac contraction (6).

*Protective Effects of Bioceramic on Ionized Radiation and Against Oxidative Stress on Human Breast Epithelial MCF-10A Cells*

Ionizing radiation, such as X-ray, alpha ray, gamma ray and cosmic rays, is a form of electromagnetic radiation. The effects of this radiation cannot be attributed to heating. The chemical and biological effects of ionizing radiation arise from two basic types of interaction. In its direct action, the radiation energy is deposited directly into its targets. In its indirect action, the external medium absorbs the radiation en-

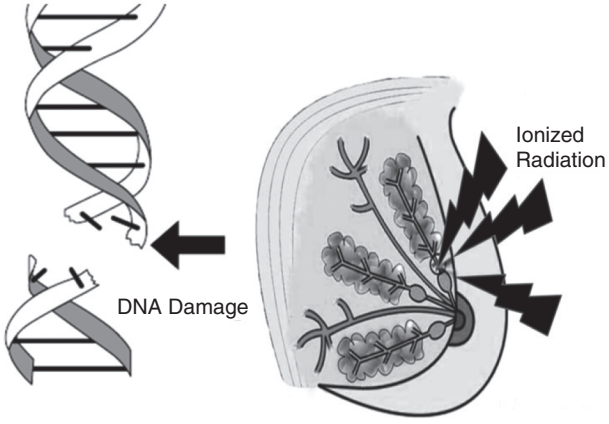


Fig. 10. Breast epithelial cell is one of the most sensitive cell types the DNA of which can be damaged by ionized radiation.

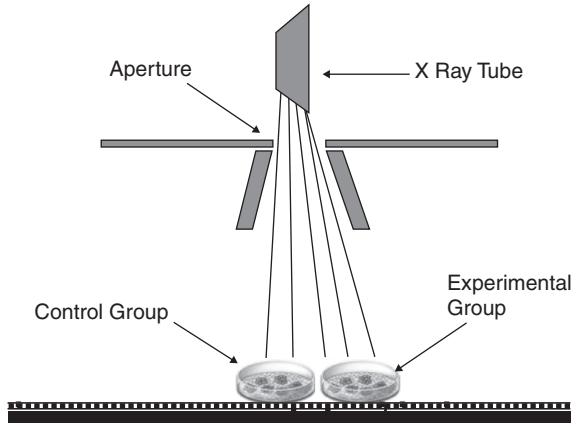


Fig. 11. Setup for X-ray exposure of cell culture discs, with the ionization source at a constant distance from the surfaces of the discs.

ergy, leading to the production of diffusive intermediates that attack the targets. Therefore, radiation damages cells directly through ionization of DNA (Fig. 10) and other cellular targets, and indirectly through reactive oxygen species (ROS), causing oxidative stress *via* free radical cellular damage. We treated MCF-10A cells with 50 μM and 100 μM $H_2O_2$ before incubating for a further 24 h beneath the Bioceramic material or a control powder. Cells were also treated with ionizing radiation from a fluoroscopic X-ray source to induce cell damage, and after culturing for a further 48 h, beneath Bioceramic material or control powder (Fig. 11), the effects of Bioceramic on cell survival were evaluated using XTT (2, 3-bis-(2-methoxy-4-nitro-5-sulfophenyl) -2H-tetrazolium-5-carboxanilide) and MTT (3-(4,5-dimethylthiazol-2-yl)-2,5 -diphenyltetrazolium bromide) assays. A total accumulated radiation dose of 1 to 2 Gy was sufficient to cause cell damage and reduce cell viability. In both the $H_2O_2$ toxicity and radiation exposure experimental models, the Bioceramic groups demonstrated significantly higher cell survival rates than the control groups ($P < 0.05$). Considering the relationship between indirect ionizing radiation- and oxidative stress-induced cell damage and the accumulation of free radicals, these results indicate that the ionizing radiation protective ability of Bioceramic occurs predominantly through an antioxidant mechanism. The study suggested that Bioceramic provides cells with a defensive mechanism during radiation exposure, and promotes cell repair during post-exposure periods through $H_2O_2$-scavenging activities. Bioceramic might have potential use in reducing radiation damage caused by medical instruments and radiation pollution. In the future, Bioceramic could also potentially contribute to public health by reducing radiation damage resulting from radiation pollution, such as the Chernobyl and Fukushima Daiichi power plant accidents (11).

## Conclusions

This article summarized our previous *in vitro* and *in vivo* studies on potential beneficial biological effects of Bioceramic, and discussed possible future clinical applications.

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