H3C HEALTH SCIENCES INNOVATION SOUVENIR

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THE EFFECT OF FERMENTED PAPAYA PREPARATION (FPP) UPON RADIOACTIVE EXPOSURE

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Background: Ionizing radiation causes cellular damage, which may lead to premature cell death or accumulation of somatic mutations which may lead to malignancy. The damage is mediated in part by free radicals, particularly reactive oxygen species. Since FPP, a product of yeast fermentation of *Carica papaya Linn.*, has been shown to act as an anti-oxidant, we studied its potential to prevent radiation-induced damage. **Methods:** FPP (0-100 µg/ml) was added either before or after irradiation (0-18 Gy) of cultured human foreskin fibroblasts and myeloid leukemia (HL-60) cells. After 1-3 days, the cells were assayed for intracellular labile iron, measured by staining with calcein, generation of reactive oxygen species, measured with dichlorofluoresceine diacetate, apoptosis, determined by phosphatidylserine exposure, membrane damage, determined by propidium iodide uptake, and cell survival – by a cell proliferation assay. DNA damage was estimated by measuring 8-oxoguanine, a parameter of DNA oxidation, using a fluorescent specific probe, and by the comet assay which measures DNA stability. These parameters were also assayed in bone marrow cells of mice treated with FPP (by adding it to the drinking water) either before or after irradiation. Somatic mutation accumulation was determined in their peripheral red blood cells, and their survival was monitored. **Results:** FPP significantly reduced the measured radiation-induced cytotoxic parameters. **Conclusions:** FPP might serve as a radio-protector. Its effect on DNA stability and mutagenicity might reduce the long-term effects of radiation, such as primary and secondary malignancy.

THE EFFECT OF FERMENTED PAPAYA PREPARATION (FPP) IN THALASSEMIA

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Oxidative stress aggravates symptoms in many diseases, including hemolytic anemias – b-thalassemia, sickle cell anemia, glucose-6-phosphate dehydrogenase, hereditary spherocytosis, congenital dyserythropoietic anaemia and Paroxysmal Nocturnal Hemoglobinuria. Although oxidative stress is not the primary etiology of these diseases, oxidative damage to their erythroid cells play a crucial role in hemolysis due to ineffective erythropoiesis in the marrow and short RBC survival in the circulation. In addition, patients with some of these diseases may experience thrombo-embolic complications and recurrent bacterial infections to which oxidative damaged platelets and leukocytes have a significant contribution. FPP, a yeast fermentation product of *Carica papaya Linn.*, has a strong antioxidant effect: We demonstrated this activity spectro-fluorometrically in a cell-free system and by flow cytometry in various blood cells. *In vitro* treatment of blood cells from b-thalassemic patients with FPP elevated their content of the main cellular anti-oxidant, reduced glutathione, and lowered reactive oxygen species, membrane lipid peroxides and external phosphatidylserine, all markers of oxidative stress, in RBC, platelets and polymorphonuclears. These effects result in (a) reduced thalassemic RBC susceptibility to hemolysis and phagocytosis by macrophages; (b) improved ability of polymorphonuclears to generate an oxidative burst – an intra-cellular mechanism of bacteriolysis, and (c) reduced platelet tendency to undergo activation. Oral administration of FPP to b-thalassemic mice (50 mg/mouse/day for 3 months) and to patients (3g x 3 times/day for 3 months) reduced the oxidative stress parameters. These results suggest that FPP, as a potent antioxidant, might alleviate symptoms in thalassemia and other forms of hemolytic anemia.

FPP IN THE STIMULATION OF RESPIRATORY BURST FUNCTION OF INNATE IMMUNE CELLS IN TYPE 2 DIABETES PATIENTS

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The World Health Organization (WHO) report that diabetes affects 346 million people worldwide. The incidence of infection is known to be increased in patients with diabetes mellitus (DM). Leukocytes (neutrophil and monocytes), through their characteristic 'respiratory burst' activity, produce superoxide anion (O2•-) and derivative reactive species which fight infection. Leukocyte NADPH oxidase, found in professional phagocytes, catalyzes the production of O2•- by the one-electron reduction of oxygen, using NADPH as the electron donor. It is widely reported that patients with type II DM (T2DM) suffer from systemic oxidative stress. However, the ability of peripheral blood monocytes of T2DM to mount respiratory burst response in response to appropriate pathogenic stimulus is known to be compromised increasing the risk of infection related complications in diabetics. Fermented papaya preparation (FPP) is a nutritional supplement reported to act as an antioxidant by scavenging reactive oxygen species (ROS) and removing 'bad ROS', while inducing "respiratory burst" production of necessary 'good ROS'. We sought to investigate the safety of oral administration of FPP (9g/d, 6 weeks) to T2D patients with respect to its effect on the hyperglycemia status of these patients. Peripheral blood was collected during a baseline visit, followed by subsequent collections during and after supplementation. Induced "respiratory burst" ROS production was measured at each visit in addition to fasting blood glucose, lipid profile, glycated hemoglobin (HbA1c), and lipid/protein peroxidation. Oral FPP supplementation induced "respiratory burst" in peripheral blood mononuclear cells while not influencing other blood parameters studied. When human monocytic THP-1 cells were supplemented with sugar-based FPP, cellular ATP and NADPH concentrations were increased while matched glucose alone did not produce similar effects, suggesting a glucose-independent component of FPP to be responsible for increasing cellular energetics. THP-1 cells supplemented with FPP also exhibited higher mitochondrial membrane potential (Äøm) and oxygen consumption as compared to cells treated with glucose alone. Taken together, our observations lead to the hypothesis that FPP corrects inducible "respiratory burst" function in type 2 diabetes patients.

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Founded in 1870 the Ohio State University commonly referred to as Ohio State or OSU, is one of the largest public research university in the United States. Ohio State's 1,764 acres (7.14 km2) of main campus is approximately 2.5 miles (4.0 km) north of Columbus's downtown. The University has an extraordinary research infrastructure and a massive research program with annual research expense close to a billion dollars. Among public schools, It ranks second in the United States on industry sponsored research.

The Ohio State University is committed to becoming a preeminent global university – one that prepares its students and faculty to participate actively in knowledge-based collaborations around the world. As one of America's best public universities, we strive to build a foundation that will integrate international dimensions with every facet of the institution, to pursue international partnerships and to collaborate on the solution of local and global issues based on Ohio State's expertise. To solidify Ohio State's commitment to enhancing its global interactions, the university has offices – Global Gateways – in key parts of the world. The India Gateway office of Ohio State in Mumbai has been the spine of all preparatory activities for the H3C. I thank the Office of International Affairs and the Wexner Medical Center for their most enthusiastic support of the H3C conference.

This H3C Health Sciences Innovation conference is co-hosted by The Ohio State University and the All India Institute of Medical Sciences. It is aimed at fostering Ohio State-India:

(i) Industry partnerships,
(ii) Academic partnerships, and
(iii) Career development opportunities

Industry partnership: (a) inviting Indian industries towards R&D partnership – from basic sciences to clinical trials; Ohio State and the State of Ohio offers its vast infrastructure to benefit Indian industries; (b) several US-based industries, many of which are currently Ohio State sponsors, are coming to India with the intent to explore business opportunities and new partnerships in India.

Academic partnership: In the area of research, education and patient care to share unique expertise in a way that value is brought to all partnering entities.

Career development: To meet Indian students and researchers (undergraduate to post-doctoral) who would like to come to Ohio State or to industries based in Ohio for education and training. To provide Ohio State students and alumni opportunities to train and gain experience in India.

During the last one year, I have had the opportunity to meet over 100 key leaders in India and the United States for the purposes of hosting H3C. The overwhelming support is reflected in the program and participating institutions. The practice of low cost health care in India is a resourceful classroom to learn from as the United States prepares to deliver affordable health care to its population.

I welcome each of you and thank you for your participation at the **H3C**. This event will seed many new partnerships that will shape the future of health care.

Chandan K Sen, PhD

"Impactful healthcare solutions may best come from borderless partnership of strengths across the globe powered by the unified spirit to serve humanity as one whole" – Chandan K. Sen (2014)

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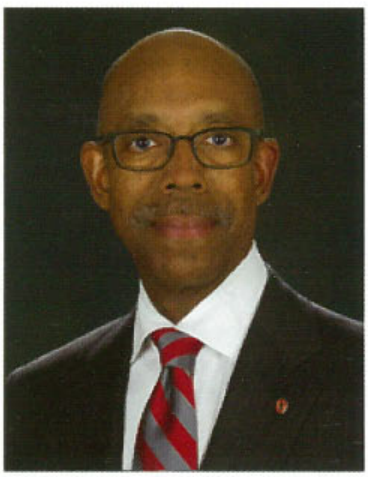

I am delighted to welcome you to the first ever OSU – India Health Sciences Innovation Conference and Trade Show. This conference is a remarkable opportunity to foster collaborative spirit between international leaders in medicine and science.

The Ohio State University is proud to host this event alongside the All India Institute of Medical Sciences (AIIMS), India's top public health care and research institution. Ohio State and AIIMS share an unwavering commitment to quality health care and research dissemination. By bringing together bright minds from around the world, the conference allows us to explore strategic industry and academic relationships, as well as career development.

Ohio State's Global Gateway in Mumbai is a key display of our dedication to supporting and working with our Indian colleagues. The office serves as a portal and resource for companies seeking to partner with the university. I am pleased that our Office of International Affairs chose Mumbai as a location to expand Ohio State's outreach and engagement, as the city is clearly a significant source of knowledge and commerce.

Just as we strive to conduct groundbreaking medical research, we must build a strong pipeline for global communication, funding and recruitment. This is essential as we seek to move forward in understanding the health sciences, and ultimately, save lives. I thank all of you for your attendance and participation in this wonderful event, and hope to see our joint efforts flourish in new and exciting ways.

Sincerely,

Michael V. Drake, MD
President
The Ohio State University

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