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Journal of the American Nutrition Association

ISSN: 2769-7061 (Print) 2769-707X (Online) Journal homepage: www.tandfonline.com/journals/uacn21

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To cite this article: Maki Osato , Okezie I. Aruoma , Keiko Nishida , Keiko Kondou , Akio Hirano , Masahiro Saito , Hirofumi Aoki & Yuki Hayashi (02 Jun 2026): Effect of Fermented Papaya Preparation Intake on Fatigue Recovery, Useful Field of View and Oxidative Stress: A Pilot Interventional Study in Professional Bus and Motor Racing Drivers, Journal of the American Nutrition Association, DOI: 10.1080/27697061.2026.2677194

To link to this article: https://doi.org/10.1080/27697061.2026.2677194

Published online: 02 Jun 2026.

JOURNAL OF THE AMERICAN NUTRITION ASSOCIATION
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Effect of Fermented Papaya Preparation Intake on Fatigue Recovery, Useful Field of View and Oxidative Stress: A Pilot Interventional Study in Professional Bus and Motor Racing Drivers

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ABSTRACT

Objectives: Fermented Papaya Preparation (FPP) is a supplement with antioxidant, anti-inflammatory, and immune-modulatory effects. This study investigated the effects of one-month continuous FPP intake on health parameters related to driving performance, the useful field of view (UFOV) and post-work fatigue recovery in active bus drivers and the effect of FPP on elite performance motor racing drivers and elite motor racing drivers.

Method: This study examined the effects of one-month continuous intake of FPP on health outcomes, oxidative stress markers and useful field of view (UFOV) in active bus drivers and elite motor racing drivers.

Result: Significant reductions were observed in oxidative stress markers (urinary 8-hydroxy-2′-deoxyguanosine [8-OHdG]) and reaction times within the UFOV. Subjective health measures related to driving performance—including concentration, vitality, fatigue, and sleep quality—also showed significant improvements. Participants with improved UFOV demonstrated concurrent reductions in urinary 8-OHdG. In the health-related quality of life assessment using the short form health survey SF-12®, significant improvements were detected in "general health perception" ($p < 0.01$), "vitality" ($p < 0.05$), and "mental health" ($p < 0.01$) after intervention. In the performance of elite drivers' assessment, the malondialdehyde (MDA) values in elite motor sport drivers were similar at the beginning of the race and at the 12 hr period, there were notable differences in the values at 24 hr following the endurance motor racing. The non-supplemented drivers had the highest level of MDA, and protein carbonyls with values of 1.26 µM and 0.411 µmoles/g protein respectively. The corresponding values for the FPP-supplemented drivers were 0.714 µM and 0.115 µmoles/g protein respectively.

Conclusion: These findings suggest that FPP can be safely consumed by professional drivers and may serve as a complementary self-care strategy targeting fatigue recovery, thereby mitigating risk factors associated with driving accidents such as age-related decline in driving useful field of view, sleep quality, cognitive function, and accumulation. FPP may be applied as a "Driver Support Tool" contributing to fatigue reduction, health maintenance, and accident risk reduction in both professional and elderly drivers. FPP may hold significance in improving recovery and cognition in elite motor sports drivers and general auto drivers.

HIGHLIGHTS OF THE FPP STUDY ON PROFESSIONAL DRIVERS

1. Fermented Papaya Preparation significantly improved fatigue-related subjective health indicators in professional bus drivers, including sleepiness, concentration, sleep quality, post-work fatigue, and feeling refreshed upon awakening after just one month of intake.
2. Fermented Papaya Preparation intake significantly reduced urinary 8-hydroxydeoxyguanosine (8-OHdG), a biomarker of oxidative stress, particularly in middle-aged and older drivers, suggesting antioxidant effects relevant to healthy aging and long-term driving performance.
3. Fermented Papaya Preparation significantly improved Useful Field of View (UFOV), especially peripheral reaction time, indicating enhanced hazard perception and visuospatial cognitive performance related to safer driving behavior.
4. The exploratory research and hypothesis-generating data from elite motor racing drivers during the 24 h of endurance motor racing indicate that supplementation with Fermented Papaya Preparation may be associated with lower oxidative stress and improved recovery under extreme conditions.
5. Fermented Papaya Preparation intake may serve as a safe and practical preventive adjunct nutraceutical approach for occupational and senior drivers to support fatigue recovery, cognitive resilience, safe mobility, and extension of "driving longevity" in aging societies.

ARTICLE HISTORY
Received 9 April 2026
Revised 8 May 2026
Accepted 16 May 2026

KEYWORDS
Useful field of view; motor sport; FPP antioxidant nutraceuticals; fatigue recovery; sport and exercise physiology; health promotion through physical exercise; sport nutrition; sport dietary supplements; fermented papaya preparation; oxidative stress; health and wellbeing; FPP and immunomodulation; professional bus drivers; elite motor racing drivers

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6. Fermented Papaya Preparation may provide adjunct beneficial benefits in the management of disease characterized by inflammation including Parkinson's disease, Alzheimer's disease, cancer, diabetes and immunological deficiencies
7. Fermented Papaya Preparation has the propensity to improve health, wellbeing and cognitive integrity aligned with healthy aging.

Introduction

Fermented Papaya Preparation (FPP) is a granulated fermented food produced by a unique long-term fermentation process of Carica papaya in Japan under rigorous international standards, including ISO 9001 (quality management), ISO 14001 (environmental management), ISO 22000 (food safety), and FSSC 22000 (food safety system certification). It has also been certified under the *Informed-Sport* program, an international anti-doping quality-assurance scheme, confirming its safety for athletes. The characteristic components of FPP are presented in Table 1, indicating potential sources of amino acids and carbohydrates (1).

Clinical and experimental studies have shown that continuous FPP intake exerts antioxidant, anti-inflammatory, and immunomodulatory effects through activation of the nuclear factor erythroid 2–related factor 2 (Nrf2) pathway (1–4). Reported benefits include improved immune function in patients with type 2 diabetes, alleviation of symptoms associated with electromagnetic hypersensitivity (fatigue, headache, insomnia, and cognitive decline such as impaired memory and concentration), and attenuation of oxidative stress and motor dysfunction in neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease (3–7). In 2025, FPP was granted a U.S. patent as a therapeutic agent for type 2 diabetes (8). Despite being carbohydrate-based, FPP does not adversely affect blood glucose levels and serves as a metabolically available energy source in diabetic mellitus.

Table 1. General composition of FPP®.

Component	Level of component per 100 g FPP
Moisture [vacuum oven method]	8.4 g
Protein[a]	0.3 g
Fat	<0.1 g
Ash	<0.1 g
Carbohydrates[b]	91.3 g
Energy[c]	366 kcal
Sodium	0.5 mg
Amino acids	
Arginine	16 mg
Lysine	6 mg
Histidine	6 mg
Phenylalanine	12 mg
Tyrosine	8 mg
Leucine	18 mg
Isoleucine	10 mg
Methioneine	5 mg
Valine	14 mg
Alanine	13 mg
Glycine	11 mg
Proline	12 mg
Glutamic acid	40 mg
Serine	11 mg
Threonine	8 mg
Aspartic acid	23 mg
Tryptophan	2 mg
Cysteine	Not detected

[a] The nitrogen to protein conversion factor was 6.25.
[b] The formula used was 100 – (moisture + protein + fat + ash); energy conversion factors were in accordance with Notification No. 176 (2003) Standards for Nutrition Labeling, Ministry of Health, Labour and Welfare, Japan.
[c] One sachet of FPP has a calorific value of 11 kcal, which is the equivalent of less than one tablespoon of cooked rice. Thus individuals with diabetes may take FPP without risks of raising level of sugar in the blood.

Exercise causes an increased oxygen consumption *in vivo*; however, a small part of the oxygen consumed leads to formation of reactive oxygen species (ROS) and reactive nitrogen species (RNS) (4–9). The metabolites of molecular oxygen include the superoxide ($O_2^{\cdot-}$), peroxyl, hydroxyl and nitric oxide radicals. The nonradical species include hypochlorous acid, hydrogen peroxide (H_2O_2), singlet oxygen, ozone, nitric oxide and nitrogen dioxide and peroxynitrite. Both ROS and RNS are important in physiological processes and can be generated by endogenous (e.g. mitochondria) or exogenous (e.g. environmental toxins) sources. Oxidative stress (the imbalance of the physiologic antioxidant mechanism and the extent of oxidative burden)-induced cell damage has been implicated in a variety of chronic diseases including cancers, diabetes, cardiovascular dysfunctions and neurodegenerative disorders such as stroke, Alzheimer's disease, and Parkinson's disease prompting the suggestion that the disease pathology can potentially be modulated by treatment with free-radical scavengers and antioxidant (10–15).

Exercise is generally advocated to be beneficial for the prevention of hypertension, heart disease, type 2 diabetes, depression and osteoporosis (16). Booth and Roberts observed that "higher aerobic capacity and often higher skeletal muscle strength are associated with a lower prevalence of most chronic diseases" and that "maintenance of aerobic capacity and skeletal muscle strength by lifelong physical activity delays the biological aging in most organ systems, therefore delaying premature death". The question as to whether associations between high aerobic capacity and muscle strength are causally or associatively related to either metabolic health or elite performance was then raised (16). Cotman et al (17) and Hillman et al (18) have argued that physical activity might improve cognition and hence delay age-related memory decline. Strategies for such intervention and prevention require an understanding of the basic molecular mechanism(s) of prophylactic agents (dietary antioxidant factors from food plants and medicinal plants in this context) that may potentially prevent or reverse the promotion or progression of the diseases. In performance sport, the level of dopamine is known to rise. Dopamine is another potential source of endogenous ROS formation (4,5, 19,20). Oxidative stress occurs because of decreased antioxidant systems (prevented by the over-expression of SOD-1) and an increase in nigral iron content. FPP reduces the extent of oxidative stress in the brain of spontaneously hypertensive rats (21) thus supporting the argument that FPP could have an important prophylactic potential in neurodegenerative diseases and in particular diseases of overt inflammation, implying that conditions that expose the human body to oxidative stress can be harmonized by FPP (1,2).

In recent years, the transportation industry has faced a shortage of professional drivers, including those operating trucks, buses, and taxis—largely due to workforce aging. With the increasing global demand for logistics, the professional driver shortage has become a pressing issue. Two major factors accelerating the driver shortage are the aging workforce and the declining number of young workers. Among the several factors, age-related declines in driving performance, delayed fatigue recovery, and increasing health risks have heightened the need for comprehensive, endogenous approaches to occupational health management that extend beyond external assessment tools such as driving simulators. Safe driving is dependent on the preservation of visual and cognitive abilities (22–26) and this is associated with aging impacting the ability to perform certain critical tasks such as driving. This study investigated the effects of one-month continuous FPP intake on health parameters related to driving performance specifically, the useful field of view (UFOV) and post-work fatigue recovery in active bus drivers (27,28). It is widely recognized that executing a maneuver that requires precise tracking of vehicle position such as turning, braking or merging, in the presence of potential conflicts such as dangerous maneuvers of other road users including pedestrians crossing the intersection, is dependent on the drivers to divide attention timely and effectively. Aging triggers a series of changes in the ocular structures, including a marked loss of lens transparency, which causes a significant increase in light scattering by the eye's optical media (29–31). Vision occurs when light is processed by the eye and interpreted by the brain. As light passes through the transparent eye surface (cornea), it continues through the pupil, the opening to the inside of the eye. The pupil becomes larger or smaller to control the amount of light that enters the eye. The iris muscle controls pupil size. After light passes through your pupil reaches the lens where it is focused on the retina (the back of the eye). The retina converts light energy into a nerve signal that the optic nerve carries to the brain, where it is interpreted. This sequence in driving is impeccably controlled. Aging causes universal ocular structural changes, including lens stiffening, pupil shrinkage, and reduced photoreceptor density—resulting in decreased visual acuity, diminished contrast sensitivity, slower dark adaptation, and conditions like presbyopia and cataracts. Indeed, aging can affect all the senses but usually hearing and vision are most affected (29–31). The study aims to contribute to the development of a sustainable occupational health framework enabling professional drivers to maintain long-term safety and well-being, representing a pioneering effort to evaluate preventive nutritional interventions at a pre-symptomatic stage. The effect of FPP on the performance of elite motor racing drivers was investigated.

Materials and methods

Participants

This study enrolled 23 active bus drivers (20 men and 3 women; age range, 22–61 years; mean age, 49.6 years) employed by the Izu Hakone Bus Company, Japan. The study was conducted between December 2024 and March 2025. All participants received both oral and written explanations of the study's objectives and procedures. They were informed that participation was voluntary, withdrawal could occur at any time without consequence to their employment evaluation or status, and privacy would be strictly protected. Written informed consent was obtained from all participants prior to inclusion. The study protocol was approved by the Ethics Committees of the Osato Research Institute and Nagoya University, Japan.

Study design

This was a prospective, single-arm intervention study designed to evaluate the effects of continuous intake of FPP on fatigue and health-related indices in healthy professional drivers using noninvasive measures. Participants consumed FPP (3 g per serving, three times daily—upon waking, during work hours, and before bedtime; total 9 g/day) for one month. Assessments were performed 2 wk before intake (Day −14), at start (Day 0), after 2 wk (Day 14), and after 4 wk (Day 28). The mean of Day −14 and Day 0 values was defined as the baseline.

Professional bust drivers questionnaire survey

Subjective health status was assessed using a self-administered 15-item questionnaire addressing awakening, sleepiness, concentration, fatigue, and sleep quality, rated on a five-point Likert scale to evaluate perceived fatigue symptoms related to work. Health-related quality of life (QOL) was assessed using the 12-Item Short Form Health Survey (SF-12®). Questionnaires were anonymized, and each participant was assigned a unique identification number to enable longitudinal tracking.

Biomarker measurements

Urinary 8-hydroxy-2′-deoxyguanosine (8-OHdG) levels and salivary amylase activity and cortisol concentration were measured as biomarkers of physical and psychological stress. Urine samples were collected upon waking, stored at −20 °C, and analyzed at the Japan Institute for Aging Control. Saliva samples were obtained immediately before visual field testing after reporting to work, stored at −20 °C, and analyzed at the Osato Research Institute using a salivary amylase monitor (Nipro Co., Japan) and a Cortisol Salivary Immunoassay Kit (Salimetrics LLC, USA).

Useful field of view (UFOV) test

Dynamic useful visual field performance was assessed using a tablet-based UFOV test application (iPad Air, 10.9-inch display). The test can be conducted at a desk and measures cognitive processing speed related to both central and peripheral vision. Participants fixed on a central dot (representing a preceding vehicle) while attending to eight peripheral dots arranged on an outer ring (representing pedestrians, traffic signals, or roadside objects). During testing, either the central or peripheral dot randomly expanded, and participants were instructed to tap the "center" or "periphery" button immediately upon detecting the change. The reaction time from stimulus onset to response was recorded separately for central and peripheral visual targets as an index of cognitive processing speed.

Motor sport endurance performance

Two groups of elite professional motor racing drivers ($n = 3$ aged 33–42 yrs and weighing 63–72 kg) with the Aston Martin Racing team Prodrive, took part in this study conducted during the Le-Mans 2007 24 hr race. The IRB for the FPP and Performance Sport Le Mans 24 hr race study was approved by the Touro College's School of Health Science (Memo Approval of Revision 1319) to assess antioxidants and cognitive integrity of motor racing drivers, and the race mechanics was Sport. The drivers were not controlled for their diet however they maintained their routine dietary habit consisting of the consumption of pasta, rice, chicken, meats, vegetables, cereals and bread with consumption of adequate water and carbonated soda. The supplemented group ($n = 2$) consumed FPP, and the non-blinded control ($n = 1$) did not. The participants received full details of the study and signed a consent form prior to commencement of the study. FPP supplied in Fort box (60 sachets), each sachet containing 4.5 g of FPP was consumed 14 days before the race.

The FPP supplemented drivers took between meals in the morning one sachet 4.5 g and in the afternoon one sachet 4.5 g (9 g/day). During the race, drivers were supplemented with 6 g FPP (2 × 3 g sachets) and at 8 hrs time intervals (maximum consumption of 18 g) during the 24 hr race. The drivers consumed water during the race period as needed and had light food following each on the race stints. Urine samples were collected to ensure compliance (given the conditions imposed by the logistics of racetrack and pit management). This was preferred as a 24-h sample collection was not a 5-practical option for the racing drivers. Thus 50 ml of urine sample was collected before the start of the 24 hr race, at the 12 hr time point and immediately after the race. Samples were stored in liquid nitrogen until analysis. The levels of malondialdehyde and protein carbonyl were measured as markers of oxidative damage. Biochemical determinations malondialdehyde (MDA) assay in urine. Urine aliquots were diluted to 25% (v/v) with water prior to use. 100 µl of dilute urine samples were mixed with 750 µl of the thiobarbituric acid reagent (TBA, 800 mg/l dissolved in 80 ml of 1.5 M NaOH) and incubated in a water bath maintained at 95 °C for 1 h. Tetraethoxypropane standards at concentrations of 0, 1, 2, 3, 4, 5 and 6 µM were similarly treated. The resulting mixtures were centrifuged. The supernatants were neutralized at pH 6–7 and analyzed with HPLC using a mobile phase containing potassium dehydrogenate buffer (10 mM, pH 6.0) with 17% (v/v) acetonitrile. 50 µl aliquots of the chromogen were injected onto an Adsorb sphere C18 column (5 µ, 250 × 4.6 mm internal diameter). Protein carbonyls Aliquots (5 ml) of the urine samples were centrifuged at 3000 g for 10 min. Aliquots (0.5 ml) of the supernatant were mixed with 1 ml of 10% (w/v) trichloroacetic acid, followed by the addition of 1 ml of 2 M HCl and 1 ml of 10% (w/v) 2,4-dinitrophenylhydrazine in the respective test tubes. The 2,4dinitrophenylhydrazine reacts with the carbonyl groups of the damaged protein. Albumin standards were similarly treated as with the urine samples. The optical density was measured at 280 nm for standards and measurement tubes. Protein carbonyl concentrations were calculated from a standard calibration curve.

Results

Subjective health indicators

Of the 23 participants enrolled, data from 21 individuals was included in the final analysis. After one month of continuous FPP intake, significant improvements were observed in multiple subjective health parameters assessed using a self-administered fatigue questionnaire. Notably, significant improvements were found in "feeling refreshed upon awakening" ($p < 0.01$); "daytime sleepiness," "lack of concentration," "irritability," and "fatigue during work" ($p < 0.05$–0.01); "post-work fatigue" and "sleep quality" ($p < 0.01$); "headache, low back pain, and shoulder stiffness" ($p < 0.05$); and "craving for sweets" ($p < 0.05$) compared with baseline (Figure 1). "Bowel movement regularity" and "ease of falling asleep" also showed significant improvement at 2 wk but not at 4 wk ($p < 0.05$ vs. baseline).

In the health-related QOL assessment using the SF-12®, significant improvements were detected in "general health perception" ($p < 0.01$), "vitality" ($p < 0.05$), and "mental health" ($p < 0.01$) after intervention (Figure 2). Furthermore, mean post-intervention scores for "general health," "vitality," "social functioning," and "mental health" exceeded the Japanese population norms.

Biomarker indicators

Urinary 8-hydroxy-2′-deoxyguanosine (8-OHdG) levels decreased in 13 of 21 participants (61.9%), showing an overall downward trend (Figure 3a). Among the eight participants (38.1%) who exhibited increased levels, five remained within the reference range established by Japan Institute for the Control of Aging (4.6–23.6 ng/kg/h). The group demonstrated a significant reduction in urinary 8-OHdG between 2 wk and 4 wk after initiation (Figure 3b, $p = 0.039$, Day 14 vs. Day 28). Participants aged ≥ 45 years initially exhibited higher 8-OHdG levels compared with younger participants; however, after one month, their levels decreased below those of the younger group (Figure 3c, $p = 0.035$, Day 14 vs. Day 28).

Salivary amylase activity decreased in 9 of 21 participants (42.9%) but did not reach statistical significance (Figure 4). Among the 12 participants who showed an increase, seven remained within the normal range (≤ 45 KU/L). Salivary cortisol concentrations decreased in 9 of 20 participants (45.0%), though the overall change was not significant

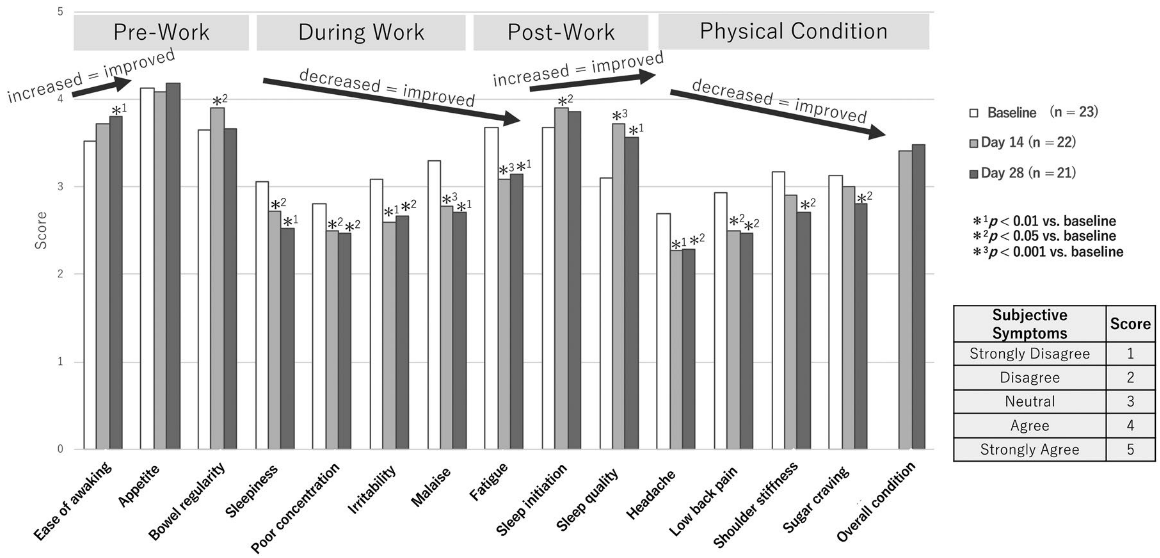


Figure 1. Improvement of subjective symptoms following 1 month of FPP intake.

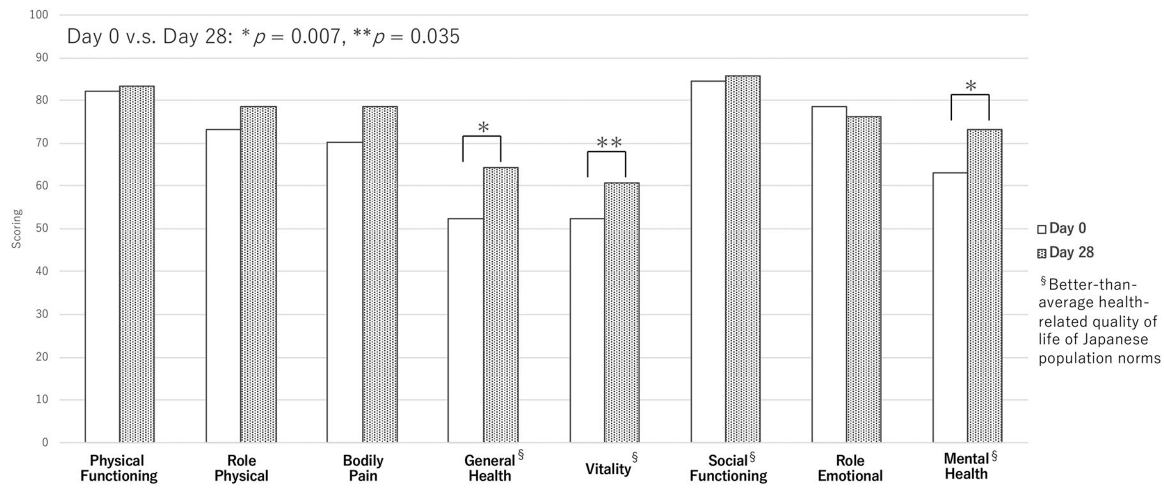


Figure 2. Changes in health-related quality of life (SF-12®) following 1 month of FPP intake ($n = 21$).

(Figure 5); five of the 11 participants showing increases remained within the reference range (0.149–0.739 µg/dL).

Useful field of view (UFOV)

The result outcome in Figure 6, indicate improvement in changes in reaction time in the central UFOV: baseline vs. after 1 month of FPP intake ($n = 2$, $p = 0.25$). After one month of continuous FPP intake, a significant improvement in reaction time was observed within the peripheral visual field (Figure 7, $p = 0.047$ vs. Day 0). Shortened reaction times were recorded in 17 of 21 participants (81.0%), including improvements in both central and peripheral fields ($n = 10$), central field only ($n = 3$), and peripheral field only ($n = 4$) (Table 2). Four participants showed no improvement in either field or exhibited prolonged reaction times. Furthermore, participants demonstrating improvements in either the central field alone or in both the central and peripheral visual fields showed significant reductions in urinary 8-OHdG (Figure 8, $p = 0.044$). Among those with improved UFOV performance, 11 of 17 participants (64.7%) exhibited decreased 8-OHdG levels, compared with only 1 of 4 (25.0%) among those without UFOV improvement. No significant correlations were found between UFOV performance and salivary amylase activity or cortisol

Motorsport 24 hr Le Mans race

Due to the race specifics and restrictions, urine samples were obtained from the elite drivers at the specified collection times. The urinary markers of oxidative stress, MDA, protein carbonyls were measured in 3 elite racing drivers during the 2007 Le Mans 24 hr race. Samples were taken before the race, at 12 hrs and after the race (Figure 9A and B). The MDA values were similar at the beginning of the race and at the 12 hr period, however there were notable differences in the MDA value at 24 hr following the race. The non-supplemented driver had higher level of MDA and protein carbonyls used as marker of oxidative protein damage (Figure 9). The non-supplemented driver had the highest level of MDA and

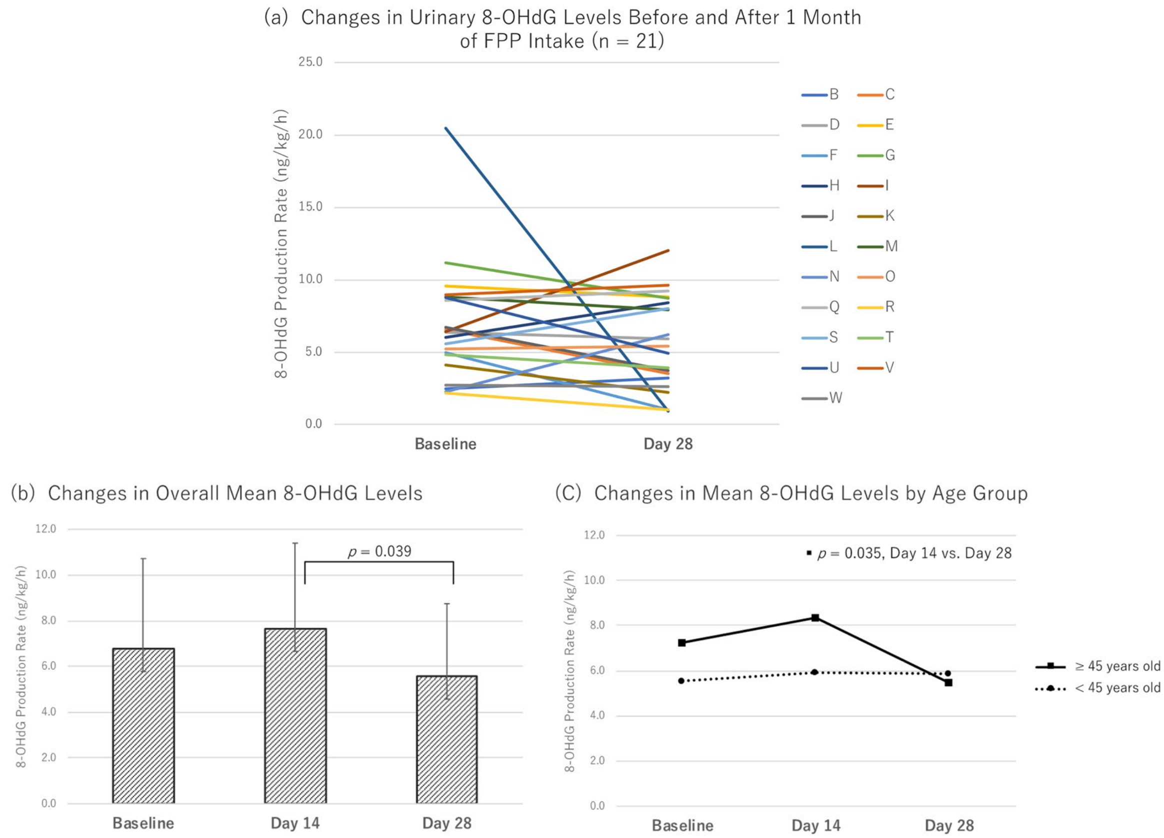


Figure 3. Changes in urinary 8-OHdG levels: (a) Baseline vs. after 1 month of FPP intake (b) Mean values in all participants (c) Mean values by age group ($n = 21$).

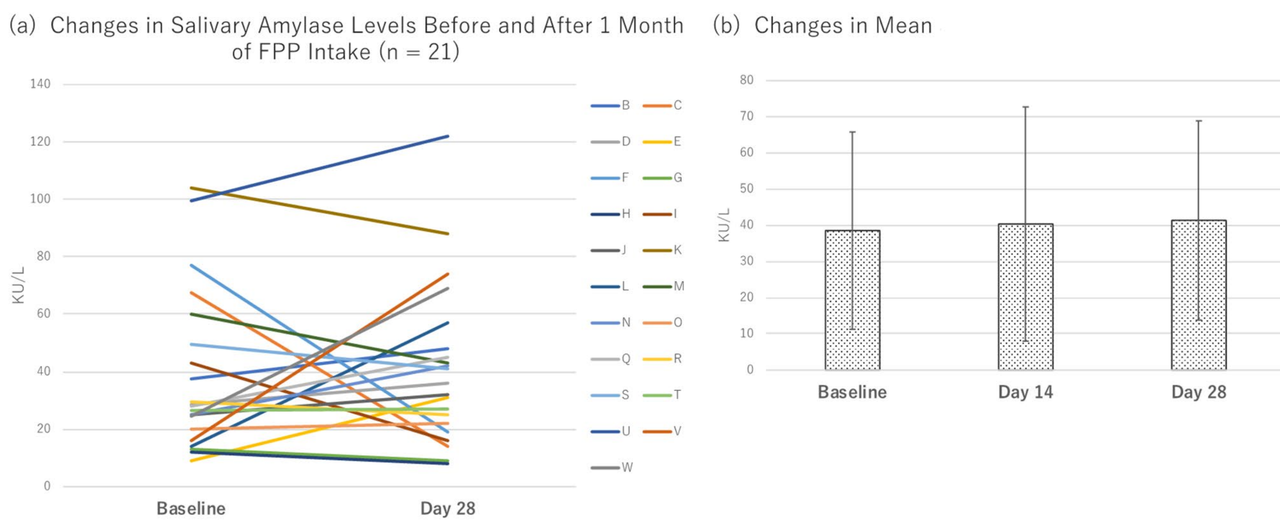


Figure 4. Changes in salivary amylase levels: (a) Baseline vs. after 1 month of FPP intake (b) Mean values in all participants ($n = 21$).

protein carbonyl with values after the 24 hr race of 1.26 µM and 0.411 µmoles/g protein respectively. The corresponding values for the FPP-supplemented drivers ranged from 0.56 −0.87 µM for MDA (Figure 9A) and 0.087–0.142 µmoles/g protein for the protein carbonyl level (Figure 9B). The sample size in this study is not enough to conduct a statistical analysis. For this reason, we are planning an extended study with larger number of elite motor racing drivers and teams. It is anticipated that the result here will be an impetus for major race teams in the USA, Europe (Great Britain, France, Germany, Italy), Japan and Asia and South America to consider participating, when the logistics of the racing events are considered. This will not only look at the oxidative stress biomarkers and molecular markers but focus on the quality of life and behavior measures with an outcome that will define the benefit of dietary supplementation in elite sports.

Discussion

Inflammation, cellular and redox signaling mechanisms have been implicated in the pathophysiology of neurodegenerative disorders such as stroke, Alzheimer's disease, and Parkinson's

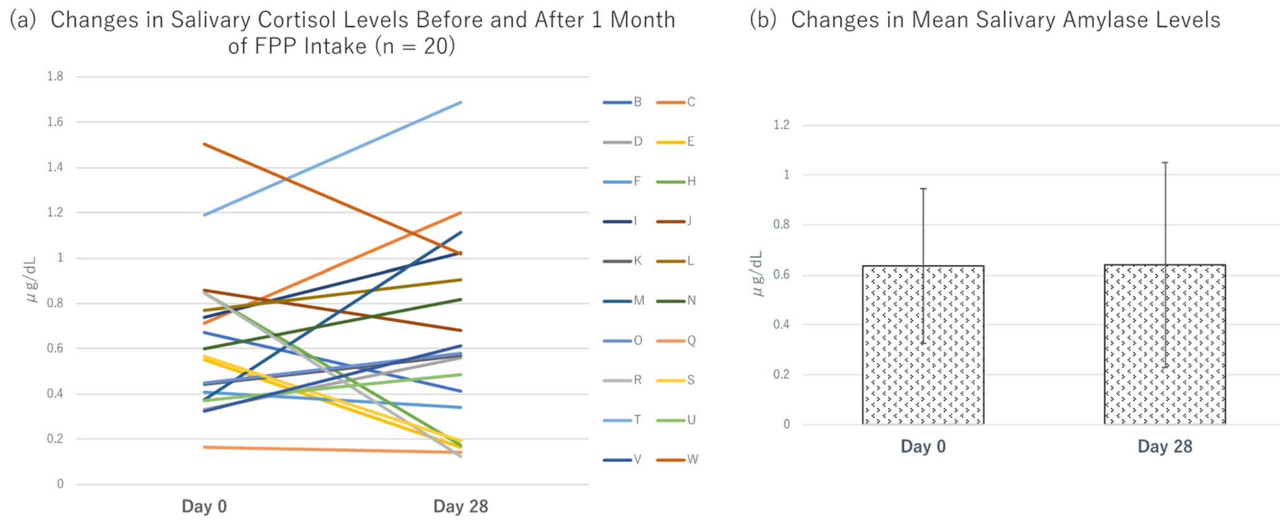


Figure 5. Changes in salivary cortisol levels: (a) Baseline vs. after 1 month of FPP intake (b) Mean values in all participants ($n=20$).

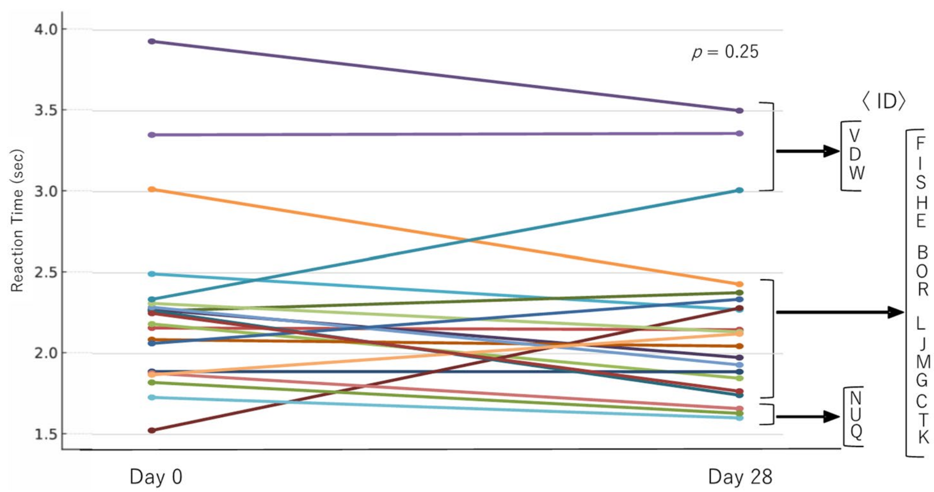


Figure 6. Changes in reaction time in the central UFOV: baseline vs. after 1 month of FPP intake ($n=21$).

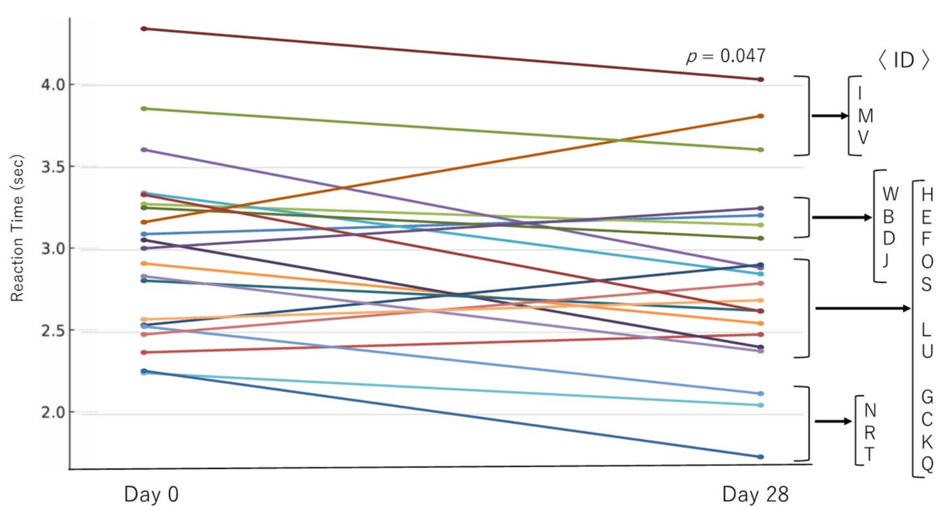
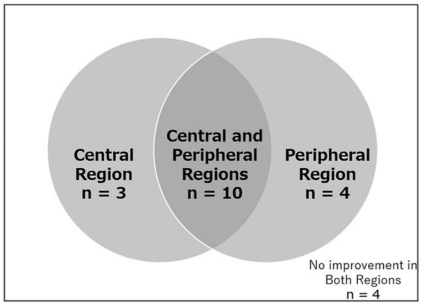


Figure 7. Changes in reaction time in the peripheral UFOV: baseline vs. after 1 month of FPP intake.

Table 2. Improvement in reaction time within the UFOV after 1 month of FPP intake.

Improvement in Reaction Time within the Useful Field
of View after 1 Month of FPP Intake



Improvements in UFOV	n
Central and Peripheral Regions	10
Central Region	3
Peripheral Region	4
No improvement in Both Regions	4
Total	21

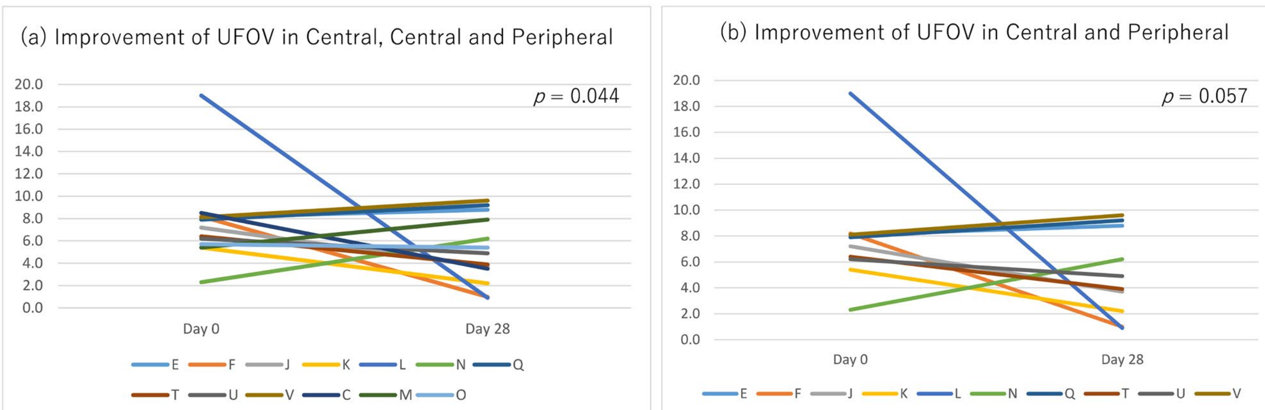


Figure 8. Relationship between reaction time in the UFOV and 8-OHdG levels: (a) 8-OHdG levels significantly decreased in both the central-only and central and peripheral improvement groups ($p = 0.044$). (b) The group with improvements in both visual fields showed a trend toward a significant decrease ($p = 0.057$).

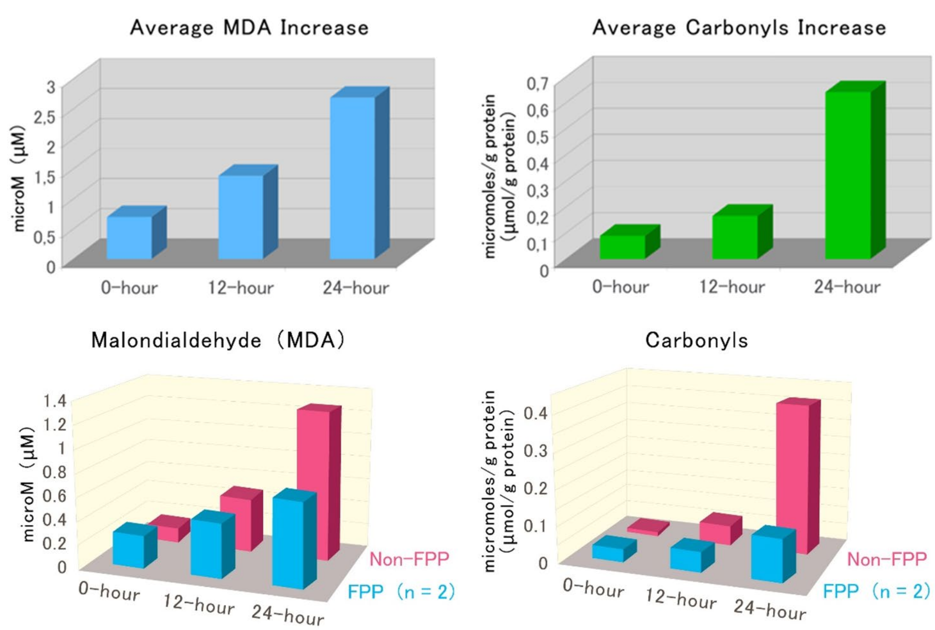


Figure 9. Changes in oxidative stress markers during the 24-h race: (a) Time-Dependent Increase in Oxidative Stress (b) Reduction of oxidative stress among FPP-supplemented drivers (FPP, $n = 2$, non-FPP, $n = 1$) The study involving professional motor racing drivers was conducted during the 24 h of Le Mans in collaboration with Aston Martin Racing team. According to Fédération Internationale de l'Automobile regulations, each car must be driven by a team of three drivers. In this highly competitive environment, where race performance is the top priority, it was not feasible to include multiple cars particularly the lead (primary) car for the exploratory interventional study. Therefore, this initial investigation was conducted using a single secondary car, comprising three drivers.

disease prompting the suggestion that the disease pathology can potentially be modulated by treatment with free-radical scavengers and antioxidant. Strategies for such intervention and prevention require an understanding of the basic molecular mechanism(s) of prophylactic agents (including dietary antioxidant factors from food plants and medicinal plants) that may potentially prevent or reverse the promotion or progression of diseases. Defining if the presence of oxidative stress in various diseases and how these could be attenuated by the administration of antioxidant compounds in food plants coupled with establishing the relationship to the presence of genetic polymorphism and modulation of the complex cell signaling cascades involving gene transcription remains a major future scientific challenge. Fermented papaya preparation has the propensity to be a unique nutraceutical agent for the management of chronic inflammation, as may be ascribed to aging (1,32). Age-related changes in vision, physical functioning, and the ability to reason and remember, as well as diseases and medications, might affect some older adults' driving abilities. This study demonstrated that one month of continuous intake of FPP improved subjective health indicators, reduced oxidative stress markers, and enhanced an aspect of cognitive function—namely, the useful field of view (UFOV)—in professional bus drivers. Because FPP is a food-based supplement, previous interventional studies have typically employed longer intake periods. However, given the demanding and schedule-restricted nature of professional driving, a one-month intervention was designed to ensure practicality and compliance. The results indicated that FPP was safe and potentially beneficial for maintaining drivers' health and performance, thereby contributing to accident prevention and occupational safety.

Significant improvements were observed in subjective parameters related to driving performance, such as sleepiness, concentration, fatigue, sleep quality, and feeling refreshed upon awakening. Sleep quality is closely linked to immune homeostasis and plays an essential role in infection defense and inflammation regulation. Sleep deprivation impairs both innate and adaptive immune functions and elevates circulating levels of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), which are implicated in the pathogenesis of chronic conditions including cardiovascular, autoimmune, and neurodegenerative diseases. FPP has previously been shown to decrease IL-6 and TNF-α levels in healthy elderly individuals, demonstrating its anti-inflammatory and immunomodulatory effects (15). In the present study, the SF-12® assessment revealed significant improvements in general health perception, vitality, and mental health, indicating enhancement of both physical and psychological well-being (23–28). These findings suggest that continuous FPP intake may help alleviate chronic fatigue and psychological stress among professional drivers, contributing to better quality of life (QOL) and long-term health maintenance through fatigue recovery.

Although urinary 8-hydroxy-2′-deoxyguanosine (8-OHdG) values remained within normal limits due to the inclusion of healthy participants, an age-related increase was observed at baseline. Remarkably, despite the short intervention period, FPP significantly reduced oxidative stress in middle-aged and older participants, confirming its antioxidant efficacy (32–36). Oxidative stress contributes to the development of numerous chronic inflammatory diseases, including atherosclerosis, cerebro- and cardiovascular disorders, glaucoma, autoimmune diseases, and neurodegenerative conditions such as Alzheimer's and Parkinson's disease (6,36–40). Therefore, the marked reduction of urinary 8-OHdG in middle-aged participants compared with younger counterparts suggests a preventive potential of FPP against oxidative stress–related disorders and supports its role in maintaining safe and sustained driving performance.

Salivary amylase and cortisol, indicators of psychological stress, did not show significant changes. This may reflect the participants' stable mental condition during the study or the influence of variability in sample collection times due to shift work. The UFOV test revealed a significant improvement in reaction time in the peripheral visual field, with 81.0% of participants showing improvement in at least one visual domain. Shortened peripheral reaction times imply enhanced spatial awareness, potentially contributing to earlier hazard detection and safer driving behavior. Importantly, 64.7% of participants with improved UFOV also exhibited decreased urinary 8-OHdG levels, suggesting a relationship between reduced oxidative stress and improved visual-cognitive performance. This finding highlights urinary 8-OHdG as a promising biochemical indicator reflecting both decline and recovery of visual field function (a novel insight derived from this study).

For participants who showed no improvement in UFOV or oxidative stress markers, future studies with larger sample sizes and extended intervention durations may clarify the influence of confounding factors such as work environment and baseline health status. Moreover, the observed improvements in visuospatial processing suggest that FPP may help sustain higher-order cognitive functions—such as traffic sign recognition, situational judgment, and rapid decision-making—that are essential for professional drivers. These functions directly relate to alertness, responsiveness, and accident prevention.

Previous research on FPP has reported attenuation of oxidative stress under acute stress conditions in professional racing drivers: the results of the two supplemented drivers show that FPP significantly protects them against increase of oxidative stress comparatively of the non-supplemented driver. The present study extends these findings to a population under chronic physical and psychological strain—professional bus drivers—demonstrating that FPP may contribute to fatigue reduction, QOL enhancement, and preservation of driving ability.

Furthermore, improvements in subjective symptoms such as reduced drowsiness and fatigue, enhanced concentration and sleep quality, and alleviation of physical discomfort (headache, shoulder stiffness, etc.) are closely associated with alertness, cognitive performance, and responsiveness during driving. These outcomes collectively suggest that FPP may serve not only as a safe self-care option for health maintenance but also as a complementary intervention for promoting safe driving and preventing traffic accidents. The parallel with the motor sport performance study is striking.

The 24 h of Le Mans race (France) is one of the World Endurance Championship that attracts the best drivers and biggest manufacturers in motorsport to the championship. The Le Mans 24 hr race is a very demanding sporting event and the process of identifying drivers that will take part in a study such as this precluded larger numbers and the extent of the investigations. Without doubt, the is one of the most challenging races for any motor racing driver. Negotiating the race circuit at speeds over 300 km/h demands extreme concentration from the driver. Motor racing involves a variety of psycho-emotional stress activities that are associated with catecholamine release, increased number of isometric contractions and oxygen consumption. The benefits of exercise and the mechanisms of tissue injury in humans are very complex and defining the role played by oxidative stress and nutrition in the process is an area of increasing interest. The traditional notion holds that excessive free radicals and oxidants (leading to oxidative stress when the level of endogenous antioxidant protection is overwhelmed) and ensuing damage from reactions involving them are detrimental. However, data are beginning to emerge to show that optimal prooxidant status can serve to up-regulate antioxidant defenses. Humans are complex in their anticipated responses during exercise.

The emotive psychology of endurance in elite performance sport (such as motor racing) presents numerous variables (including cognition and normalization of the same. There is however a need to balance training optimization (and the actual event performance) with nutrition. The work reported here supports the merit for nutritional supplements but the general nutritional strategies to optimize performance and enhance recovery. From the standpoint of antioxidant supplementation to minimize tissue injury, it is necessary to first validate the index of such injury and then develop universal methods for measuring free radical generation in humans during exercise (26–29). There is increased lipid and protein oxidation that elevates the levels of malondialdehyde and protein carbonyls as well as other markers of oxidative stress in exercise. Although FPP in this study would have modulated the extent of oxidative damage in the supplemented drivers, the extent of the benefits of supplementation of antioxidant nutrients in exercise has had mixed outcomes and it is becoming apparent that the mechanism of action of the antioxidant nutrients may reside in their ability to modulate signaling mechanisms and that this may bring about specific cellular adaptations.

The limitations that may be argued for the elite motor sports part of this study may reflect favorably for it. The study involving professional motor racing drivers was conducted during the 24 h of Le Mans in collaboration with Aston Martin Racing (AMR). According to Fédération Internationale de l'Automobile (FIA) regulations, each car must be driven by a team of three drivers. In this highly competitive environment, where race performance is the top priority, it was not feasible to include multiple cars particularly the lead (primary) car for the exploratory interventional study. Therefore, this initial investigation was conducted using a single secondary car, comprising three drivers. We acknowledge that a sample size of three is insufficient for conventional statistical analysis. However, this limitation is inherent to studies involving rare and highly specialized populations. A similar challenge is well recognized in research involving astronauts, where small sample sizes often preclude the detection of statistically significant differences, even when meaningful physiological effects are present. In such contexts, it is considered appropriate to place greater emphasis on effect size, consistency of response, and biological plausibility, rather than solely on statistical significance. Accordingly, the findings from the motor racing drivers in this study should be interpreted as exploratory and hypothesis-generating, providing supportive evidence alongside the larger dataset obtained from professional bus drivers.

Motor racing drivers are under immense pressure during the race such that certain sample collection measures that were intended were not possible (for example taking blood samples). The data presented is the first of its kind for elite motor racing drivers. The observation that the levels of MDA and protein carbonyls as markers of oxidative stress were markedly lower in the FPP-supplemented drivers is important. The net effect of antioxidant supplementation on oxidative stress environment is to spare the utilization of endogenous antioxidants such as glutathione and to modulate gene expression whereupon the levels of the antioxidant enzymes glutathione peroxidase, superoxide dismutase and catalase as well as the integrity of protein thiols are modulated, principally contributing to the homeostatic balance *in vivo*. The wellbeing of the drivers is of critical importance given the psycho-emotional pressures in performance sports.

The FPP-supplemented drivers reported improved recovery rate following the race stints of about 2 hr, feeling less fatigued, being less emotionally drained, and feeling alert during the more difficult night driving sessions during the 24 hr race. The non-supplemented driver, however, felt both physically and mentally tired and noticed the tiresomeness toward the early morning hours even with 8–9 h more to the end. The FPP-supplemented drivers who would normally be exhausted a day after the race reported feeling less mentally drained and well rested after a night's sleep and were able to recover more quickly. These observations require validation derived from large scale studies with elite motor racing drivers in future planned studies to involve several motor sport teams and car manufacturers. The aim will be to corroborate the appropriate quality of life and behavior questionnaires with the biomarker's outcome in elite motor sports. While the number of participants in the present was limited (again due to the practical difficulty in getting consent from the motor racing team management for this study) the difference of oxidative stress parameters level at end of race between the FPP-supplemented and no supplemented drivers is important. The implication for the elite drivers is that higher fatigue and more muscle oxidative attack (stiffness, cramps) due to the exhaustive exercise could be modulated by supplementation with FPP.

Conclusion

Specifically, the study seeks to clarify the effects of a functional food, FPP® (Fermented Papaya Preparation), on mental and physical functions, physiological indicators, and subjective evaluations related to driving performance in senior professional drivers.

The implication for the elite motor racing drivers and performance sports athletes is that higher fatigue (including stiffness and cramps) and oxidative stress burden due to the exhaustive exercise could be modulated by supplementation with dietary FPP. That FPP may be contributing to biological adaptation mediating the upregulation of antioxidant defense systems (and hence homeostasis) in performance and elite sport is a point that extended future studies will define. FPP thus represents a preventive adjunct nutraceutical approach that combines safety, practicality, and efficacy, supporting health preservation at the pre-disease stage. A large-scale clinical study is currently underway in collaboration with the University of Florida to investigate whether FPP can enhance driving performance among community-dwelling elderly drivers aged 70-80 years. The present findings provide foundational evidence that FPP may help maintain driving ability in middle-aged and older adults by facilitating fatigue recovery. Considering that automobile use is essential for independent living in rural areas, these results highlight FPP's potential societal value in promoting safe mobility and extending healthy longevity among older populations.

Acknowledgement

The authors express their sincere gratitude to the bus drivers and the Operations Management Division of the IZUHAKONE Bus Co., LTD. for their kind cooperation and support throughout this study. We are grateful to the Aston Martin Racing Team England and their elite drivers who participated in the study. We are grateful to Pierre Mantello, Catherine Garrel, and Henri Faure, University Hospital, Grenoble, France for assistance with the analysis of the elite motor racing samples.

Author contributions

CRediT: **Maki Osato**: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing; **Okezie I. Aruoma**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing; **Keiko Nishida**: Data curation, Investigation; **Keiko Kondou**: Data curation, Investigation; **Akio Hirano**: Data curation, Formal Analysis, Investigation; **Masahiro Saito**: Data Curation, Investigation, Project Administration, Resources, Supervision; **Hirofumi Aoki**: Data curation, Formal analysis, Investigation, Methodology, Resources, Supervision, Validation; **Yuki Hayashi**: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – review & editing.

Disclosure statement

Maki Osato and Yuki Hayashi are affiliated with the Foundation Osato Research Institute. Okezie I. Aruoma is a Consultant for the Foundation Osato Research Institute. No potential conflict of interest was reported by other authors.

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