

**FERMENTED PAPAYA PREPARATION SUPPLEMENTATION:  
EFFECT ON OXIDATIVE STRESS TO ISOLATED RAT HEARTS.**

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Received July 7, 1995

Fermented Papaya Preparation (F.P.P.), a natural health food product prepared by yeast fermentation of medicinal plants, has been recently reported to possess antioxidant properties. To better define its antioxidant action, we investigated the effects of orally supplemented F.P.P. on oxidative damage in the rat heart. Hearts were isolated from control or F.P.P. supplemented animals and 1) exposed to ischemia-reperfusion using the Langendorff technique, or 2) homogenized and exposed to peroxy radicals generated from (2,2'-azobis (2,4-dimethylvaleronitrile) (AMVN). During reperfusion following 40 minutes of ischemia, leakage of lactate dehydrogenase from hearts isolated from F.P.P. supplemented rats was significantly lower than from hearts of control animals. Furthermore, lower levels of AMVN-induced accumulation of thiobarbituric acid reactive substances and of protein carbonyl derivatives were measured in homogenates prepared from hearts isolated from F.P.P. supplemented rats than in samples from control animals. Our findings confirm an antioxidant action of F.P.P. and show that it protects the heart against ischemia-reperfusion induced damage.

### Introduction

Damage induced to cellular constituents by oxygen-derived free radicals have been accepted to play a crucial role in the pathogenesis of a wide range of chronic and degenerative disorders (aging, atherosclerosis, neurodegeneration cancer, cataract), as well as in acute clinical conditions (ischemia-reperfusion) (1). Therefore, substances with antioxidant properties have recently been given unprecedented attention as possible therapeutic and preventative agents (2).

Fermented Papaya Preparation (F.P.P.), a health food prepared from a yeast fermented mixture of medicinal plants (*Carica papaya*), has been recently reported to possess hydroxyl radical scavenging action resistant to both heat and acid treatment, from *in vitro* experiments using EPR spectroscopy (3). Evidence has also been reported for a protective effect of F.P.P. supplementation against oxidative damage in the brain with different model systems. Oral administration of F.P.P. in rats has been reported to significantly decrease the release of monoamine metabolites and the occurrence of lipid peroxidation in iron-induced epileptogenic focus in the brain (4,5).

F.P.P. supplementation was reported to increase the superoxide dismutase activity in rat brain, decrease the age-related formation of thiobarbituric acid reactive substances (TBARS), improve the physical condition of the rats and increase life span (6).

To define the antioxidant activity of a substance, it is necessary to evaluate its efficacy in a wide range of oxidative conditions. Thus, to better delineate the activity of F.P.P. against oxygen radicals-mediated injury and analyze the possibility for therapeutic use of F.P.P. against oxidative damage in tissues, we administered F.P.P. to rats and investigated the consequences of oral supplementation on *in vitro* models of oxidative stress-induced damage. Two *in vitro* model systems of oxidative damage were used: 1) ischemia-reperfusion of the Langendorff heart; 2) induced oxidation of heart homogenates by the lipid soluble azo-initiator of peroxy radicals, AMVN (2,2'-azobis(2,4-dimethylvaleronitrile).

Cardiac tissue is a well recognized target of oxidative stress. In particular ischemia-reperfusion conditions, such as those occurring during a process of myocardial infarction, are known to increase cellular damage as a result of free radical generation (7). Thus, the identification of agents able to prevent oxidative modification of cardiac tissue is an important pharmacological aim.