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Insulin Resistance and the Metabolic Syndrome Severity – a Mathematical Model

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Abstract. *Excessive fructose consumption was shown to have deleterious effects on the cardiovascular system, particularly as the metabolic syndrome. However, the degree by which alteration of each pathophysiological factor contributes to the morbidity associated with fructose consumption is not yet clear. We have developed a mathematical model to integrate and uniformly quantify pathophysiological features of the metabolic syndrome on a high fructose-fed dog model. A novel comprehensive measure for the syndrome severity (the "patholog") and a more intuitive measure of the insulin resistance are introduced. Alteration of hemodynamics, echocardiography and blood chemistry were determined in adult male mongrel dogs fed with 60% isocaloric fructose or normal chow for 7 weeks. The diverse experimental data were transformed into comparable scores and a pre-Hilbert space of states constructed. In such a space one can quantify the severity of any combination of pathophysiological and genomic features and determine the global recovery resulting from a treatment. The model indicates increase of insulin resistance (new index proposed), systolic blood pressure, low-to-high density lipids ratio and angiotensin II as the major contributors to the excessive fructose morbidity. Our model provides the simplest, yet the most intuitive and comprehensive way to integrate data of a wide diversity in visualizing and quantifying a cardiovascular disease.*

Key words: Fructose consumption, Cholesterol, Insulin resistance, Angiotensin II, Dog model

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1. Introduction

One major cause of obesity, type 2 diabetes, fatty liver and cardiovascular disease of millions in the Western world countries is the excessive sugar consumption, particularly in the form of high-fructose corn syrup [1-4]. Such consequences of the excessive fructose consumption are heralded by the metabolic syndrome [5-9], a combination of medical disorders reaching a prevalence of 35-39% in the United States [10]. According to the American Heart Association, the metabolic syndrome is characterized by: 1) increased waist circumference (men > 102 cm, women >90 cm), 2) elevated triglycerides (≥150 mg/dL), 3) reduced high density lipids (men < 40 mg/dL, women (< 50 mg/dL), 4) elevated blood pressure (≥ 130/85 mmHg), 5) elevated fasting glucose (≥ 100 mg/dL)1. High fructose diet results in hypertension [11], atherosclerosis [12], hyperurecimia [13],