International Journal of Emerging Engineering Research and Technology
Volume 3, Issue 4, April 2015, PP 37-43
ISSN 2349-4395 (Print) & ISSN 2349-4409 (Online)

Stochastic Model to Find the Effect of Glucose-Dependent Insulinotropic Hormone by Fructose Using Strongly Nonlinear Variational-Like Inequality

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ABSTRACT

The purpose of the Study was to evaluate the effect of fructose on gut hormones with focus on Glucose-dependent Insulinotropic Hormone in Nine healthy humans. The Subjects were given to drink a sugar solution containing 75 g fructose or glucose dissolved in 300 ml of water within 2 minutes. In healthy humans glucose potentially stimulated Glucose-dependent Insulinotropic Hormone but fructose was without effect. In this paper, the problem is investigated by considering auxiliary principle technique to prove the existence of a unique solution of strongly nonlinear mixed variational-like inequality.

Keywords: GIP, Gut hormone, Metabolic syndrome, Hilbert space, strongly nonlinear variational-like inequality.

2010 Mathematics Subject Classification: 60G05; 60G20; 47J20;

INTRODUCTION

The Gut is the largest hormone-producing organ of the body. While it has long been known that the presence of nutrients such as glucose, fat and protein in the intestinal lumen stimulates secretion of many gut hormones. Fructose is a major sweetener in Western diets [1] [3]. Increased dietary intake of fructose has been suspected to be partly responsible for the growing rates of obesity and the metabolic syndrome [14] [15], possibly due to fructose-induced perturbation of cell signaling and inflammatory reactions in insulin-sensitive tissues [17]. The present study to investigate the effect of fructose on appetite and metabolism-regulating hormones from the gut, with a particular focus on the incretin hormones GIP. Nine healthy humans with mean age 27.7 ± 1.2 yr, range: 23.4-36.8, mean body mass index 21.7 ± 0.4 kg/m^2, range: 18.2-26.3 participated in the study. All subjects had normal fasting blood glucose levels and none had parents or siblings diagnosed with any type of diabetes. No subjects received medication known to interfere with glucose homeostasis. Each subject was studied on two occasions within 3 wk after the first day of study. Subjects were instructed to refrain from vigorous exercise and alcohol for atleast 24 hr before each study. Study days began at 0830 proceeded by a 10-h overnight fast. Venous blood samples were collected at time -10, 0, 15, 30, 45, 60, 90, 120 min. At time 0 min subjects drank a sugar solution containing 75 g fructose or glucose dissolved in 300 ml water within 2 min. GIP concentrations did not differ between treatments at baseline ($P > 0.05$, n=9). While GIP concentrations rose significantly at 15 min after glucose ingestion (43 ± 5.0 pm, $P > 0.0001$, n=9), reaching at plateau from 15 to 120 min

($P < 0.0001$, n =9), fructose did not significantly elevate GIP concentrations ($P > 0.05$, n=9), also compared with basal levels ($P > 0.05$). GIP areas under curves were greater after glucose than fructose intake ($P < .0001$).

In this paper the problem is investigated by the auxiliary principle technique to prove the existence of solution of variational-like inequalities [12] [19]. The projection method was used to study the existence of a solution of the multivalued quasi-variational inequalities. The auxiliary principle technique [2], [6], [13], [5], [10], [11], [4] to prove the existence of a unique solution of the strongly nonlinear mixed variational-like inequality.

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Notations

H Hilbert space

Y Multivalued mapping

K(x) Convex set

f Nonlinear operator

I Identity operator

STOCHASTIC MODEL

Preliminaries

Let H be a real Hilbert space whose norm and inner product are denoted by $\|.\|$ and $\langle .,. \rangle$, respectively. Let K be a nonempty closed convex set in H. Let $Q, B, f : H \to H$ be a single-valued operators and $Y : H \to 2^H$ be a multivalued operator.

For a point-to-set mapping $K : x \to K(x)$, which associates a closed convex set $K(x)$ with any element x of H, consider the problem of finding $x \in H$ and $v \in Y(x)$ such that $f(x) \in K(x)$ and

$$\langle Qx + Bv, f(y) - f(x) \rangle \geq 0, \text{ for all } f(y) \in K(x). \tag{1}$$

A problem of type (1) is called the multivalued general nonlinear quasi-variational inequality problem. The projection method was used to study the existence of a solution of the multivalued quasi-variational inequalities. The implicit obstacle odd order boundary value problems can be studied in the general framework of quasi-variational inequalities (1), [9].

Hence in relation to multivalued general quasi variational inequality (1) we consider the problem of solving the generalized implicit Wiener-Hopf equations. Let $U_{K(x)}$ be the projection of H into $K(x)$ and $V_{K(x)} \equiv I - U_{K(x)}$, where I is the identity operator. We consider the problem of finding $z \in H, x \in H$ and $v \in Y(x)$ such that

$$Qf^{-1}U_{K(x)}z + \gamma^{-1}V_{K(x)}z = -B(v), \tag{2}$$

Where $\gamma > 0$ is a constant and f^{-1} is the inverse of the operator f. Inequality (2) is called multivalued implicit Wiener-Hopf equations. For the general treatment, formulations, and applications, [19], [18], [8].

Given single-valued nonlinear operators $Q, B : H \to H$ and $\beta : H \times H \to H$, we consider the problems of finding $x \in H$ such that $\beta(x, y) \in K \times K$ and

$$\langle Qx + B(x), \beta(y, x) \rangle + i(y) - i(x) \geq 0, \text{ for all } y \in H \tag{3}$$

Where $i : H \to H$ is a proper, semi-continuous, convex and no differentiable function. This problem is called the strongly nonlinear mixed variational-like inequality problem.

Special cases: (a). If $\beta(x, y) = y - x$, then problem (3) is equivalent to finding $x \in H$ such that

$$\langle Qx + B(x), y - x \rangle + i(y) - i(x) \geq 0, \text{ for all } y \in H \tag{4}$$

Inequality (4) is mainly due to [7].

(b). If $\beta(y, x) = f(y) - f(x)$ where $f : H \to H$ is a nonlinear operator, then (3) is equivalent to finding $x \in H$ such that $f(x) \in K$ and

$$\langle Qx + B(x), f(y) - f(x) \rangle + i(y) - i(x) \geq 0, \text{ for all } f(y) \in K \tag{5}$$

And is known as the general strongly nonlinear mixed variational inequality problem [5].

(c). If $B(x)\equiv 0$ then (3) is equivalent to finding $x\in H$ such that

$$\langle Qx,\beta(y,x)\rangle + i(y) - i(x) \ge 0 \text{ , for all } y\in H \tag{6}$$

Which is a problem considered and studied [13], where the auxiliary principle technique was used to study the existence of a unique solution and to suggest an iterative algorithm.

(d). If $i(x)\equiv 0$, then (3) reduces to finding $x\in H$ such that $\beta(x,y)\in K\times K$ and

$$\langle Qx + B(x),\beta(y,x)\rangle \ge 0 \text{, for all } y\in H \text{ .} \tag{7}$$

Inequality (7) is called the strongly nonlinear variational-like inequality [10]

The suitable choice of operators Q, B, f, Y, β and convex set $K(x)$, one can arrive various classes of variational inequalities, complementarity problems, and the Wiener-Hopf equations as special cases of (1) and (7).

Definition 2.2: The nonlinear operator $\beta : H\times H\to H$ is said to be

(i) Strongly monotone if there exists a constant $\rho > 0$ such that

$$\langle \beta(y,x), y-x\rangle \ge \rho\|y-x\|^2 \text{, for all } x,y\in H \text{ .}$$

(ii) Lipschitz continuous if there exists a constant $\sigma > 0$ such that

$$\|\beta(y,x)\| \le \sigma\|y-x\| \text{, for all } x,y\in H \text{ .}$$

If $\beta(y,x) = Qy - Qx$, where $Q : H\to H$ is a single-valued operator, then (1) reduces to the usual definition of strong monotonicity and Lipschitz continuity of nonlinear operator Q. From (i) and (ii), it follows that $\rho\le\sigma$. Note that if $\sigma = 1$, and then the operator β is no expansive.

Definition 2.3: The multivalued mapping $Y : H\to C(H)$ is called M-Lipschitz continuous if there exists a constant $\lambda > 0$ such that

$$M(Y(x),Y(y)) \le \lambda\|x-y\| \text{, for all } x,y\in H \text{ .}$$

Where $C(H)$ the family of all nonempty is compact subsets of H and $M(.,.)$ is the Hausdorff metric on

$C(H)$.

Assumption 2.4: The nonlinear operator $\beta : H\times H\to H$ satisfies the relation

$$\beta(y,x) = -\beta(x,y) \text{, for all } x,y\in H \text{ .}$$

Obviously $\beta(x,y) = 0$, for all $x\in H$, and it was used to study the existence of a solution of the variational-like inequalities [21], [22].

Lemma2.5: Let K be a closed convex set in H. Then, for a given $z\in H, x = U_K z$ if and only if $x\in K$ satisfies $\langle x-z, y-x\rangle \ge 0$ for all $y\in K$.

Furthermore, the projection operator U_K is nonexpansive, (i.e.),

$$\|U_K x - U_K y\| \le \|x-y\| \text{, for all } x,y\in H \text{ .}$$

AUXILIARY PRINCIPLE TECHNIQUE

In this section, we use the auxiliary principle technique to prove the existence of a unique solution of the strongly nonlinear mixed variational-like inequality (3).

Theorem 3.1: Let an operator $Q: H \to H$ be strongly monotone with constant $\rho > 0$ and Lipschitz continuous with constant $\sigma > 0$. Let an operator $\beta : H \times H \to H$ be strongly monotone with constant $\alpha > 0$ and Lipschitz continuous with constant $\mu > 0$. Let operator $B: H \to H$ be Lipschitz continuous with constant $\eta > 0$ and Assumption 2.4 hold. If $m < \rho$, where ρ is the strongly monotonicity constant of Q, and m is constant as defined by (12), then there exists a unique solution $x \in H$ of vatiational-like inequality (3).

Proof: (i) Uniqueness: Let $x_1, x_2 \in H, x_1 \neq x_2$ be two solutions of (3); (i.e.)

$$\langle Qx_1 + B(x_1), \beta(y, x_1)\rangle + i(y) - i(x_1) \geq 0, \text{ for all } y \in H. \tag{8}$$

and

$$\langle Qx_2 + B(x_2), \beta(y, x_2)\rangle + i(y) - i(x_2) \geq 0, \text{ for all } y \in H. \tag{9}$$

Taking $y = x_2$ (respectively x_1) in (8), performing the summation of the resultant inequalities and using the assumption that $\beta(x_1, x_2) = -\beta(x_2, x_1)$, we have

$$\langle Qx_1 - Qx_2, \beta(x_1, x_2)\rangle \leq -\langle B(x_1) - B(x_2), \beta(x_1, x_2)\rangle$$

Which can be written as

$$\langle Qx_1 - Qx_2, x_1 - x_2\rangle \leq \langle Qx_1 - Qx_2, x_1 - x_2 - \beta(x_1, x_2)\rangle - \langle B(x_1) - B(x_2), \beta(x_1, x_2)\rangle.$$

Now using the strong monotonicity and Lipschitz continuity of the operator T, we have

$$\rho\|x_1 - x_2\|^2 \leq \|Qx_1 - Qx_2\| \, \|x_1 - x_2 - \beta(x_1, x_2)\| + \|B(x_1) - B(x_2)\|\|\beta(x_1, x_2)\|$$

$$\leq \ \sigma\|x_1 - x_2 - \beta(x_1, x_2)\| + \eta\|\beta(x_1, x_2)\| \ \|x_1 - x_2\|, \tag{10}$$

Where $\eta > 0$ is the Lipschitz continuity constant of B.

Since the operator β is strongly monotone and Lipschitz continuous, it follows that

$$\|x_1 - x_2 - \beta(x_1, x_2)\|^2 = \|x_1 - x_2\|^2 - 2\langle \beta(x_1, x_2), x_1 - x_2\rangle + \|\beta(x_1, x_2)\|^2$$

$$\leq (1 - 2\alpha + \mu^2)\|x_1 - x_2\|^2 \tag{11}$$

From (10), (11) and the Lipschitz continuity of β, we get

$$\rho\|x_1 - x_2\|^2 \leq \ \sigma(\sqrt{1 - 2\alpha + \mu^2} + \eta\mu \ \|x_1 - x_2\|^2 = m\|x_1 - x_2\|^2,$$

Where

$$m = \sigma(\sqrt{1 - 2\alpha + \mu^2} + \eta\mu \tag{12}$$

Thus,

$$\rho - m \ \|x_1 - x_2\|^2 \leq 0,$$

Which implies that $x_1 = x_2$, the uniqueness of the solution, since $m < \rho$.

(ii) Existence: we now use the auxiliary principle technique, to prove the existence of a solution of the mixed variational-like inequality (3). Hence for given $x \in H$, we consider the problem of finding a unique $v \in H$ satisfying the auxiliary mixed variational-like inequality

$$\langle v, y - v\rangle + \gamma i(y) - \gamma i(v) \geq \langle x, y - v\rangle - \gamma\langle Qx + B(x), \beta(y, v)\rangle, \tag{13}$$

for all $y \in H$, where $\gamma > 0$ is a constant. Inequality (13) defines a mapping $x \to v$. In order to prove the existence of a solution of (3), it is sufficient to show that the mapping $x \to v$, defined by (13) as a fixed point belonging to H which satisfies (3). In other words it is sufficient to show that for a relevant choice of $\gamma > 0$ $\|v_1 - v_2\| \le \phi \|x_1 - x_2\|$ with $0 < \phi < 1$, where ϕ is independent of x_1 and x_2. Let v_1 and v_2 be two solutions of (13) related to x_1 and x_2, respectively. Taking $y = v_2$ (resp v_1) in (13) related to x_1 (resp x_2), we have that

$$\langle v_1, v_2 - v_1 \rangle + \gamma i(v_2) - \gamma i(v_1) \ge \langle x_1, v_2 - v_1 \rangle - \gamma \langle Qx_1 + B(x_1), \beta(v_2, v_1) \rangle \tag{14}$$

And $\langle v_2, v_1 - v_2 \rangle + \gamma i(v_1) - \gamma i(v_2) \ge \langle x_2, v_1 - v_2 \rangle - \gamma \langle Qx_2 + B(x_2), \beta(v_1, v_2) \rangle$ (15)

Adding these inequalities and using the assumption $\beta(v_1, v_2) = -\beta(v_2, v_1)$ for all $v_1, v_2 \in H$, we have

$$\langle v_1 - v_2, v_1 - v_2 \rangle \le \langle x_1 - x_2, v_1 - v_2 \rangle - \gamma \langle Qx_1 - Qx_2, \beta(v_1, v_2) \rangle - \gamma \langle B(x_1) - B(x_2), \beta(v_1, v_2) \rangle$$

$$= \langle x_1 - x_2 - \gamma(Qx_1 - Qx_2), v_1 - v_2 \rangle + \gamma \langle Qx_1 - Qx_2, v_1 - v_2 - \beta(v_1, v_2) \rangle - \gamma \langle B(x_1) - B(x_2), \beta(v_1, v_2) \rangle,$$

From which it follows that

$$\begin{aligned} \|v_1 - v_2\|^2 &\le \|x_1 - x_2 - \gamma(Qx_1 - Qx_2)\| \|v_1 - v_2\| + \gamma \|Qx_1 - Qx_2\| \|v_1 - v_2 - \beta(v_1, v_2)\| \\ &\quad + \gamma \|B(x_1) - B(x_2)\| \|\beta(v_1, v_2)\| \end{aligned} \tag{16}$$

Since Q is strongly monotone and Lipschitz continuous, therefore

$$\|x_n - x_{n-1} - \gamma(Qx_n - Qx_{n-1})\|^2$$

$$= \|x_n - x_{n-1}\|^2 - 2\gamma \langle Qx_n - Qx_{n-1}, x_n - x_{n-1} \rangle + \gamma^2 \|Qx_n - Qx_{n-1}\|^2$$

$$\le (1 - 2\gamma\rho + \sigma^2\gamma^2) \|x_n - x_{n-1}\|^2. \tag{17}$$

Combining (11), (16) and (17) and using the Lipschitz continuity of Q, B and β, we have

$$\|v_1 - v_2\| \le \sqrt{1 - 2\gamma\rho + \gamma^2\sigma^2} + \gamma(\sigma\sqrt{1 - 2\alpha + \mu^2} + \mu\eta) \ \|x_1 - x_2\|$$

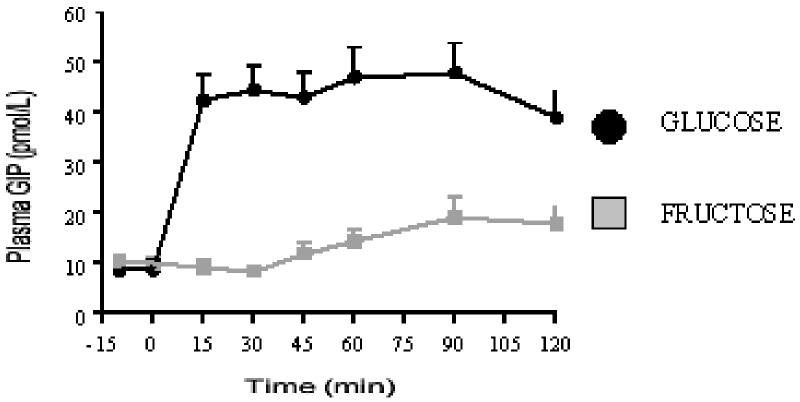
$$= r(\gamma) + \gamma m \ \|x_1 - x_2\| = \phi \|x_1 - x_2\|,$$

Where $\phi = r(\gamma) + \gamma m, r(\gamma) = \sqrt{1 - 2\gamma\rho + \sigma^2\gamma^2}$ and $m = \sigma\sqrt{1 - 2\alpha + \mu^2} + \mu\eta$.

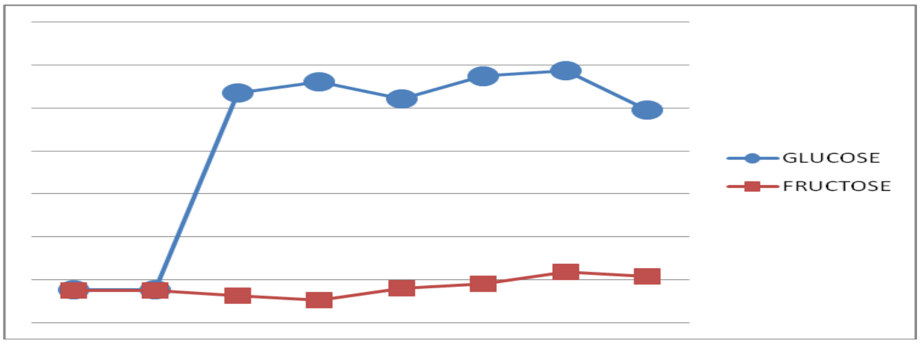
We need to show that $\phi < 1$. It is clear that $r(\gamma)$ reaches it minimum value at $\bar{\gamma} = \frac{\rho}{\sigma^2}$ with $r(\bar{\gamma}) = \sqrt{1 - \frac{\rho^2}{\sigma^2}}$. For $\gamma = \bar{\gamma}, \gamma m + r(\gamma) < 1$ implies that $\gamma m < 1$. Thus, it follows $\phi < 1$ for all γ with $0 < \gamma < 2\frac{\rho - m}{\sigma^2 - m^2}, \gamma m < 1$ and $m < \rho$. Consequently, the mapping $x \to v$ defined by (13) has a fixed point belonging to H, which is a solution of the mixed variational-like inequality (3).

EXAMPLE

The Fig. (1) Shows the GIP responses of fructose on gut hormones with focus on Glucose-dependent Insulinotropic Hormone in Nine healthy humans. Nine healthy humans with mean age 27.7 ± 1.2 yr, range: 23.4-36.8, mean body mass index 21.7 ± 0.4 kg/m^2, range: 18.2-26.3 participated in the study. All subjects had normal fasting blood glucose levels and none had parents or siblings diagnosed with any type of diabetes. No subjects received medication known to interfere with glucose homeostasis. Each subject was studied on two occasions within 3 wk after the first day of study. Subjects were instructed to refrain from vigorous exercise and alcohol for atleast 24 hr before each study. Study days began at 0830 proceeded by a 10-h overnight fast. Venous blood samples were collected at time -10, 0, 15, 30, 45, 60, 90, 120 min. At time 0 min subjects drank a sugar solution containing 75 g fructose or glucose dissolved in 300 ml water within 2 minutes in healthy human's glucose potentially stimulated Glucose-dependent Insulinotropic Hormone but fructose was without effect [16].



Fig(1)



Fig(2)

CONCLUSION

Evaluation of the GIP responses of fructose on gut hormones with focus on Glucose-dependent Insulinotropic Hormone in Nine healthy humans. The Subjects were given to drink a sugar solution containing 75 g fructose or glucose dissolved in 300 ml of water within 2 min. In healthy humans glucose potentially stimulated Glucose-dependent Insulinotropic Hormone but fructose was without effect. In this paper the problem is investigated by the auxiliary principle technique to prove the existence of solution of variational-like inequalities. The result coincides with the mathematical and medical report.

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