

# Prevention of Stress-Induced Ulcers in Rats Occur Via Absorption of Glucose and Fructose in Their Gastric Mucosa

STRETEKİ RA TIKARIN MİDE MUKOZA IA RIND AN GL UKOZ VE ERUKTOZ ABSORBE OLUR VE ÜLSER OLUŞMASINI ÖNLENMESİ

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## SUMMARY

*Hyperosmolar solutions such as glucose 25% and other nutrients prevent stress-induced ulcers in rats, if they were given to stomach by a nasogastric tube. There are various explanations about the prophylactic effects of these solutions. We had investigated the prophylactic effects of honey and hyperosmolar glucose on the stress induced ulcers in rats the gastric absorption of glucose and fructose in the gastric mucosa were measured in the rats. The study was performed with 30 rats. Various solutions were given into their stomach by catheter during the experiment. Absorption rates of glucose and fructose were measured in the gastric mucosa of rats which were given honey of 30%, glucose of 30%, fructose of 30% and fructose of 10%. The absorption rates of glucose and fructose were 55.2%-57.1%, 63.8%, 65.3% and 89.5% for the above mentioned solutions respectively and the averages of the macroscopic lesions were 1.57+, 0.80+, 0.83+, 0.63+ and 0.50+ in the groups given serum physiologic, honey, glucose and 30% and 10% solutions. It was concluded that absorption of glucose and fructose occurs in the gastric mucosa of rats in restraint and therefore prevents stress-induced ulcers.*

**Key Words:** Stress ulcers, Glucose, Fructose

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## ÖZET

*Çeşitli hiperosmolar solüsyonların, rotlarda stresle oluşturulan ülserleri imlediği bilinir. Bu solüsyonların profilaktik etkileri hakkında birçok açıklama vardır. Bu çalışmada, glukoz ve fruktozun stres ülserinde koruyucu etkileri ve mide mukozasından absorpsiyonları araştırıldı. Deneyde 30 rat kullanıldı. Deney süresince kaleler aracılığı ile ratların midelerine değişik solüsyonları verildi. %30'luk bal, %30'luk glukoz, %30'luk fruktoz ve %10'luk fruktoz solüsyonları verilen ratların mide mukozalarından glukoz ve fruktozun absorpsiyon oranları tespit edildi. Yukarıdaki sıraya göre değişik solüsyonları verilen rotlarda glukoz ve fruktozun absorpsiyon oranları %55.2-%57.1, %63.5, %65.3 ve %89.5 idi. Mide mukozalarında gelişen makroskopik lezyonların ortalamaları ise, serum fizyolojik verilenlerde 1.57+, %30 bal verilenlerde 0.80+, %30 glukoz verilenlerde 0.83+, %30 fruktoz verilenlerde 0.63+ ve %10 fruktoz verilenlerde 0.50+ idi. Stresteki rotların mide mukozasından glukoz ve fruktozun absorbe olduğu ve böylece strese bağlı ülser gelişmesini önlediği sonucuna varıldı.*

**Anahtar Kelimeler:** Stres ülserleri, Glukoz, Fruktoz

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**Acute gastric mucosal lesions may develop in patients with major burns, multiple injuries, sepsis, etc. If bleedings occur depending on these lesions, mortality rate is upper than 40% (11) Different types of the prophylactic methods are offered for these lesions. Every type of methods aims less mortality and morbidity. Looking for the best method**

have been continued up till now. Intravenous solutions, including electrolytes and nutritional supplements, antacids, H<sub>2</sub> receptor blockers and solutions which were given to the stomach and including protein, fat and carbohydrates in various concentrations were attempted for this purpose. The prophylactic effects of these methods had been found more superior on the stress-induced ulcers, respectively (12,19,23).

We had investigated the prophylactic effects of honey and hyperosmolar glucose on the stress-induced ulcers in rats and established the superiority of honey with our previous study (22). When we investigated reasons of this superiority, in literature, we found some papers which argue that glucose may be absorbed in the gastric mucosa, but they had not proved it (2,9) or opposite thought (18).

Because of these reasons, we have performed this study to investigate absorption or not of fructose and glucose from the gastric mucosa and the protective effects of these substances on the stress-induced ulcers in rats.

## MATERIAL AND METHODS

Study was performed with 30 Swiss-albino type rats weighing 140-200 gr. All rats were conditioned for two months on standard rat chow and water. Prior to each experiment the rats were fasted 24 hours except for water. After a light anaesthesia with ether in the glass jar, their abdomen were opened with upper median incision. Cardia and pylor of stomachs were ligated. A polyethylene tube (feeding tube number one) was inserted into the stomach on the prepyloric region. Tube was taken out through the incision. The abdomen was closed with interrupted silk sutures. The rats were settled in stress cage and given first dose (1 ml) of test solutions (3 ml of solution was given to the stomach and taken back 2 ml of solution for first sample) by the tube. The experiment was performed by the persons unaware of the treatment. The cages were hanged up in refrigerator for four hours. The test solutions were prepared in this way, water was added on the 3 gr honey (Honey 30%) or on 3 gr fructose "Merck" (Fructose 30%) or on 1 gr fructose "Merck" (Fructose 10%) up to 10 ml in the Biochemistry Department. From these prepared solutions and glucose 30% "Eczacıbaşı" and serum physiologic were given 1 ml per hour. So, total 4 ml of solution had been given into the stomach along the restraint. At the end of each experiment the rats were taken out from

the cages. They were sacrificed by an intracardiac injection of sodium pentobarbital. All of the gastric contents were aspirated, the volume and the contents of glucose and fructose were measured. Measurement of fructose/glucose was performed from samples, by enzymatic method. Reagents of the enzymatic determination of D glucose/D fructose "Boehringer, 139106" were used and read spectrophotometrically at 340 nm.

The stomach of each animal was removed, opened along the greater curvature and spread out on the blocks of paraffin and examined lesions under a dissecting microscope by pathologist unaware of the treatment group. Bleeding lesions greater than 0.5 mm were counted individually. Patches of mucosal erythema were noted separately and graded: 1+ if less than five discrete areas were counted, 2+ if more than four lesions were counted but less than one third of the mucosa was affected, and 3+ if one third or more of the mucosa showed abnormal erythema. If there were no lesion and mucosal erythema graded "0". Statistical analyses were done by Student's unpaired t test.

## RESULTS

At the end of the experiment, twenty-six rats were alive. Two rats died at fourth hour of the experiment in the group of 30% Glucose. Two deaths were in the group of serum physiologic. One died at 3 th hour and the other one died at 4 th hour of the experiment.

Glucose of fructose absorption rates in the groups that were given honey, glucose 30%, fructose 30% and fructose 10%, were 55.2%-57.1%, 63.8%, 65.3% and 89.5% respectively. According to statistical analysis, there were significant differences between the group which was given 10% fructose and the others ( $p < 001$ ) (Figure 1).

In the macroscopic evaluations of the stomachs; 0.50+ gastric lesions occurred in the group fructose 10% and this grade was the lowest, but gastric absorption was the highest in this group (89.5%). The largest mucosal lesions occurred in the serum physiologic group. The average of mucosal lesions was 1.57+ in this group. Averages of mucosal lesions were 0.83+ in the glucose 30%. 0.63+ in the fructose 30% and 0.80+ in the honey group. The group given fructose 10% was different from the others according to statistical analysis ( $p < 0.001$ ) (Figure 1).

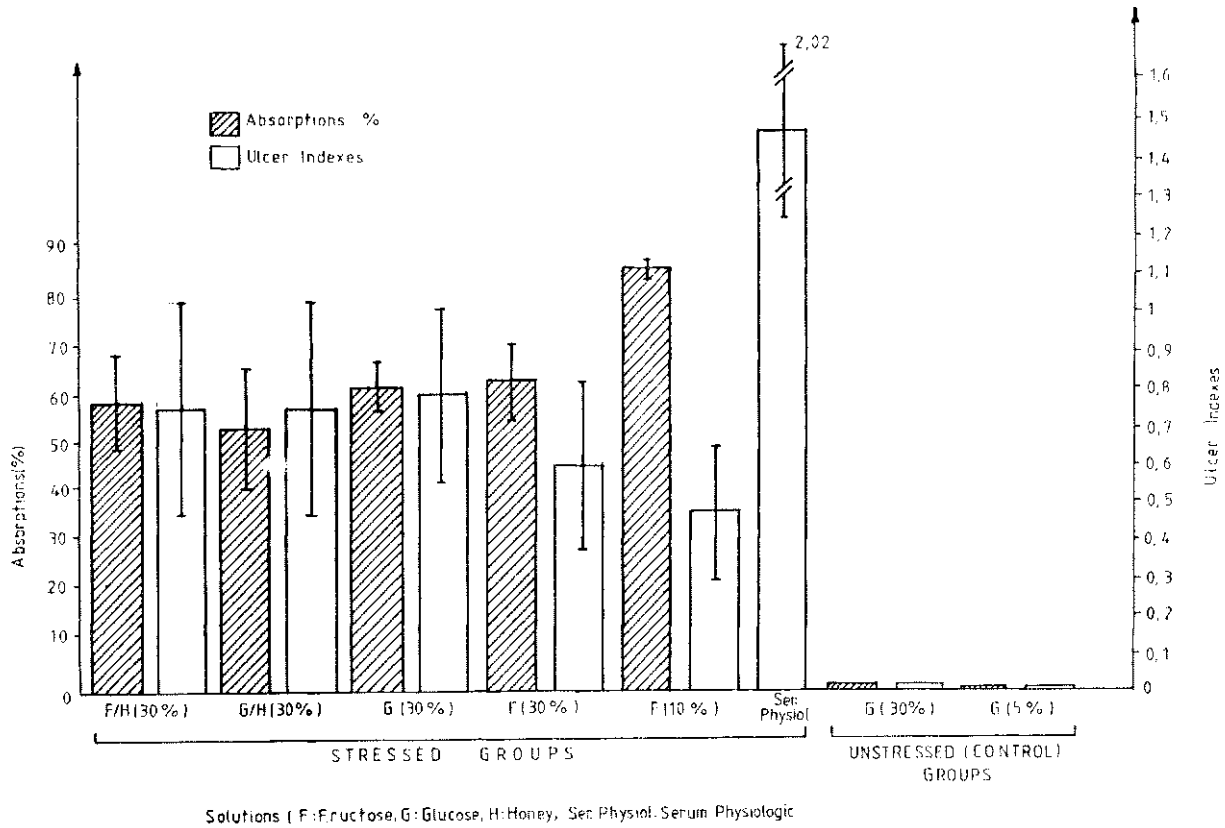


Figure I, Absorption rates of glucose, fructose and ulcer indexes in groups.

**Table 1. Glucose and Fructose Absorption Rates From the Stomach and Ulcer Indexes in The Rats**

Groups (Stressed)	n	Absorption % Ulcer Indexes	
		Arithmetical Means and S.D	
I. Fructose (Honey 30%)	6	58.08 ± 9.55	0.80 ± 0.24
Glucose (Honey 30%)	6	55.22 ± 12.46	0.80 ± 0.24
II. Glucose (30%)	6	63.86 ± 4.83	0.83 ± 0.27
III. Fructose (30%)	6	89.47 ± 1.62'	0.50 ± 0.15
V. Serum Physiologic	6		1.57 ± 0.45*
<b>Groups (Unstressed, Control)</b>			
VI. Glucose (30%)	6	0.36 ± 0.36***	0.50 ± 0.10
VII. Glucose (5%)	6	0.22 ± 0.22***	0.30 ± 0.14

\* Statistical significance of differences between group IV and IF  
\*\* group V and the others, "'groups VI. VII and the others

**DISCUSSION**

Although the mechanism of the stress induced ulcers is not clear, the effects such as secretion of gastric acid (17), mucosal ischemia (7), deficiency of metabolic energy (14) and vasoactive substances as histamin and serotonin due to increasing of H + permeability (8) as the possible causes of the ulcers.

Menguy et al (13) determined the levels of adenosine triphosphate, adenosine diphosphate and adenosine monophosphate, glucose 1-P, glucose 6-P, lactate, pyruvate and glycogen in the gastric glandular mucosa, liver and skeletal muscle in the shock induced rats. They showed that energy deficit in the gastric mucosa was more severe than

the liver and the skeletal muscle was not affected in this regard. At the end of their experiments, they suggested that the extraordinary vulnerability of gastric mucosal energy metabolism to shock-induced ischemia results from the lack of glycogen in this tissue.

Kevin P. Lally et al (9) evaluated various nutritional supplements and cimctidinc in the prevention of stress-induced gastric ulcers in rats. They showed that any solution providing calorics, including 25 patient glucos solution, afforded significant protection against ulceration. While the antacids were better than no treatment, they were significantly worse than any nutritional supplement. They explained the gastric defence of the rat to have markedly increased by absorption of the luminal substrates. The existence of an "alkaline mucus" layer lining the gastric mucosa that may function as a protective barrier was proposed by both Schierbeck and Pavlov 90 years ago [4]. Hcatlcy (6) emphasized the true importance of the role that mucus adherent to the luminal surface of the gastric epithelium might play in gastric defence with his studies.

In studies with porcine gastric mucus, this substance was noted to be a water-insoluble visco elastic gel that consists of a polymer of glycoprotein molecules bound together by disulfide bridges. Human gastric mucus has been shown to have a comparable composition. It is now known that glycoprotein matrix effectively prevents permeation of pepsin and other large molecules and also impedes hydrogen ion diffusion (15). Bicarbonate secretion is important between this mucus layer and mucosa in mucosa defence. On the other hand, there is a pump that secures  $H^+$  ion flux to the lumen from mucosa and  $Na^+$  ion flux to the mucosa from lumen. So, all of the above events contribute to the mucosal integrity and are energy-mediated processes (3).

In the stress induced ulcers, the synthesis of mucus is inhibited, the gastric mucosal barrier is broken,  $Na^+/H^+$  pump works inadequately,  $H^+$  is fluxed back to the mucosa, histamin appears in the gastric mucosa so occur local vasospasm, necrose and ulcers due to deficit of energy in the mucosa (3,4,6,15).

The normal mucosal barrier may prevent the absorption of carbohydrates as glucose and fructose.

Mullanc JF and Wilfong RG (IS) showed that glucose was not absorbed in the normal gastric mucosa. But, we can expect the absorblion of glucose and fructose if the mucus barrier is disrupted. It is known that glucose was absorbed by active transport and fructose was absorbed by active transport and fructose was absorbed by facilitated diffuision in the gastrointestinal mucosa (5). We found that fructose and glucose had been absorbed up to 55% from the gastric lumen with this study. In this study, there were significant differences in the absorption of fructose among the groups of 10% fructose, 30% fructose and honey. We suggest that this consequence is due to the differences of saturations.

According to macroscopic evaluations of the stomach, we noticed that there were hyperemia and congestion on the gastric mucosa of rats which were given hyperosmolar glucose, fructose and honey. Robert (21) suggested that hyperosmolar solutions increase endogen prostaglandins (PG12) in the gastric mucosa if they were given in the stomach. Miller and Jacobson (16) stated that prostaglandins increase gastric flow. Although we did not measure the levels of prostaglandins in the gastric mucosa, we thought hyperemia and congestion of gastric mucosa of rats that were given hyperosmolar solutions and honey come from the increase of endogen prostaglandins. Chaudhury (1) had similar opinions as ours. This observation called our attention to the other way of the protective effect of hyperosmolar solutions on stress-induced ulcers. Character of metabolism is as important as lacking of energy sources in the development of stress induced ulcers. Gastric vasoconstruclion occurs as we explained them above. Decreased energy sources could not be utilized adequately, because there were plenty of LDH isoenzymes al some regions of the stomach. Crcbs cycle does not work, energy is provided only by pyruvate-lactate pathway (20). We can suggest that hyperosmolar solutions decrease hipoksemia by endogen prostaglandins, in the cellular metabolism, crebs cycle works more effectively, so these substances may protect gastric mucosa on stress-induced ulcers in the rats.

We can now discuss, why ulcers did not happen as much as in previous study, So we did not see the prophylactic effects of solutions clearly and could not find a difference between the groups. We

can explain it because we performed the experiments in the different methods. Our goal was to show if absorption of glucose and fructose occurred or not in the stomach. That is why we ligated pylor and carida of the stomach. We had injured the vagus nerve and had prevented reflux of the bile salts and enzymes of pancreas to the stomach. So, We eliminated two objects of the aggressive factors (7-10). Therefore, we obtained low ulcer index.

As a result, we have shown hyperosmolar glucose, fructose and honey which were given into the stomach, prevented stress-induced ulcers and were absorbed in the gastric mucosa in this study.

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