



## Preventive Effect of Flavonoids on Glucose Absorption from the small Intestine in Rats with Experimental Pancreatitis

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### Abstract

The preventive effect of flavonoids such as rutin, dihydroquercetin, pulicaron and tamiflazide on the absorption of glucose from solutions of starch, maltose, sucrose, and glucose in the small intestine at acute pancreatitis was studied in experiments on Wistar rats. Flavonoids were administered intragastrically at a dose of 20 mg/kg for 5 days before the induction of experimental pancreatitis. Experimental pancreatitis was induced by administration of L-arginine at a dose of 500 mg/100 g body weight at 12-hour intervals. It turned out that experimental pancreatitis led to inhibition of glucose absorption from 0,2% starch solutions as well as from 2% maltose, sucrose and glucose solution in the isolated small intestine segment. Rutin, dihydroquercetin and tamiflazide prevented inhibition of glucose absorption from the small intestine caused by pancreatitis from all substrates. Pulicaron did not have any preventive effect on the repression of glucose absorption from the small intestine. Consequently, rutin, dihydroquercetin and tamiflazide can be used as anti-pancreatic drugs for prevention of glucose inhibition absorption in the small intestine.

**Keywords:** Small Intestine; Starch; Disaccharides; Glucose Saccharide; Absorption; Rutin; Dihydroquercetin; Pulicaron; Tamiflazide

### Introduction

The study of the absorption of glucose, supplied with food or formed as a result of hydrolysis of nutrients, from the small intestine into the internal environment of the body is one of the pressing problems of physiology [1]. There are a number of works devoted to the study of glucose absorption from the cavity of the small intestine in diabetes mellitus and its correction with medicinal plants [1,2]. However, the question of changes in glucose absorption from the small intestine in other diseases of the pancreas, for example in acute pancreatitis, remains open.

In recent years, due to the progressive spread of pancreatitis [3], the need has arisen all over the world to solve problems associated with the prevention and correction of this dangerous disease. Due to the fact that drug treatment is nonspecific and mainly aimed at relieving pain that occurs during the disease [4], non-invasive treatment or prevention of the disease based on restorative therapy is in demand. In this regard, the development of harmless means of preventing pancreatitis began to attract the attention of experts.

Flavonoids are known as a group of substances with broad preventive and therapeutic properties which have a number of health

benefits. Flavonoids are rich in antioxidants involved in the body's natural immune defense against environmental and endogenous toxins. Some flavonoids have several significant biological activities, such as anticancer, antibacterial, antifungal, anti-stress, anti-inflammatory, anti-diabetic, neuroprotective, cardioprotective. Many food flavonoids enter the cavity of gastrointestinal tract [5]. Therefore, the use of flavonoids for the correction and prevention of various diseases and their complications, including the absorption of glucose at pancreatitis has prospects.

The purpose of this work is to study the preventive effect of some flavonoids on the absorption of glucose in the small intestine.

### Material and Methods

Outbred male rats weighing  $200.0 \pm 20.0$  g were used in experiments. Rats were kept in plastic cages 4 animals each in natural light and humidity and room temperature. Animals were fed with the vivarium diet with unlimited access to water and food. Water and food were changed daily at the same time from 9.00 to 10.00 a.m.

In the study, all experimental rats were divided into four groups of six rats each. Rats of the 1st group were used as "positive" con-

trol. They were processed instead of various drugs used in the experiment with saline solution using appropriate methods, at the same time and in an equivalent volume.

Rats of the 2<sup>nd</sup> group were served as a “negative” control group. They were injected intraperitoneally with L-arginine saline solution (500 mg/100g/12h) twice. The 2<sup>nd</sup> group of animal also was taken saline (0, 5 ml) intragastrically instead of during 5 days before experimental pancreatitis. The same model of experimental pancreatitis was used in 3<sup>rd</sup>, 4<sup>th</sup>, 5<sup>th</sup> and 6<sup>th</sup> animal groups.

3<sup>rd</sup> group of rats received a solution of rutin (Rt) dissolved in 1% dimethyl sulfoxide solution (20 mg/kg/24 h) intragastrically for 5 days before inducing L-arginine pancreatitis.

In the 4<sup>th</sup>, 5<sup>th</sup> and 6<sup>th</sup> animal groups, dihydroquercetin (Dhq), pulicaron (Pl) and tamiflazide (Tm) (20 mg/kg/24 h) dissolved in physiological solution were administered intragastrically for 5 days before acute pancreatitis. Rats were sacrificed by decapitation 3 days after L-arginine administration.

### Absorption of glucose

Glucose absorption from the rat intestinal cavity into the blood was determined *in situ* condition under nembutal (60 mg/kg) anesthesia.

For determined glucose absorption abdominal cavity of anesthetized rats was opened, and a 20 cm long part from the beginning of jejunum was isolated using ligatures. Plastic catheters were inserted into both sides of the isolated intestine, and the jejunum segment was washed with 5 ml of saline warmed to 37°C from the proximal side to the distal side. Carbohydrate substrate solution were introduced into the jejunum segment and incubated for 30 minutes. To study glucose absorption from the intestine a separate rat was used for each carbohydrate substrate. Absorption of monomer from saccharides was assessed by change of glucose concentration in the blood. The glucose concentration was measured in the rat tail blood at the 15<sup>th</sup> and 30<sup>th</sup> minutes of substrate incubation in a jejunum segment. For that after local novocain anesthesia tip of the rats’ tail was incised with a sharp scalpel and the glucose concentration was determined in the resulting blood drop using a glucometer Satellite (Russia).

The experiment was performed in strict compliance with international bioethics rules of the Helsinki Declaration of the World Medical Association 2010 [6].

### Statistics

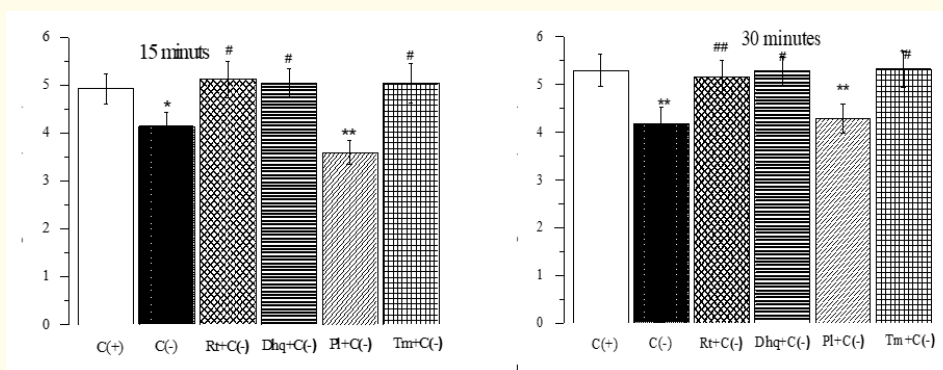
The obtained results were processed using Origin 6.1 program. Arithmetic mean value (M), standard error ( $\pm m$ ), Student’s coefficient (t) and statistical significance coefficient (P) were determined. At  $P < 0.05$ , the results are considered statistically reliable.

## Results and their Discussion

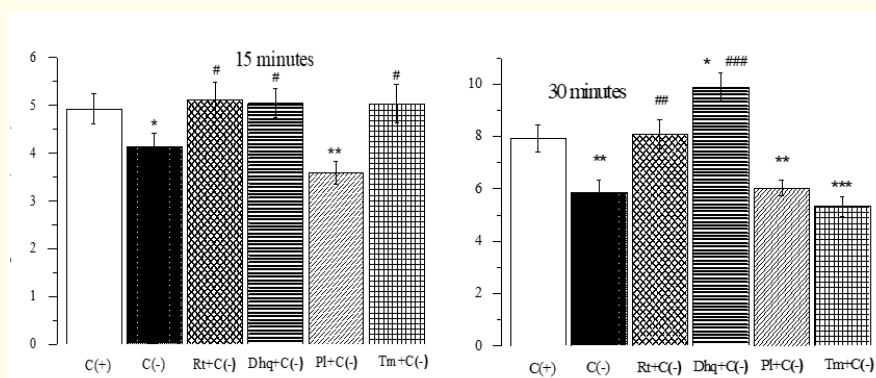
- **Absorption of glucose from starch and glucose solution:** In experimental pancreatitis, the absorption of glucose in blood from jejunum cavity starch solution decreased by 16.1%, at the 15<sup>th</sup> minute and by 21.1% at the 30<sup>th</sup> minute of observation. When animals were administered Rt, Dhq and Tm before inducing experimental pancreatitis, the transition of starch glucose from the jejunum cavity segment into the blood circulation remained at the level of the positive control in both observation times. For pulicaron, no prophylactic effect was observed (Figure 1).
- **Absorption of glucose from maltose solution:** In animals with experimental pancreatitis, after 15 and 30 minutes incubation in the jejunum segment the absorption of glucose from maltose into the blood decreased by 17.1% and 26.2%, respectively, according to the results of the positive control (Figure 2).
- In this case, also, the inhibitory effect of the disease on glucose absorption was not observed at the 15<sup>th</sup> and 30<sup>th</sup> minute of observation if the animals were administered Rt, Dhq and Tm before experimental pancreatitis. Under the influence of Dhq the absorption of glucose from maltose even increased above the indicator of the positive control at the 30<sup>th</sup> minute of observation. There was no preventive effect of pulicaron on the transition of glucose from maltose into the hemocirculation in animals with pathology (Figure 2).
- **Absorption of glucose from sucrose solution:** In experimental pancreatitis, the absorption of glucose from a sucrose solution in the intestinal cavity decreased by 47.2% at the 15<sup>th</sup> minute of observation, and by 37.5% at the 30<sup>th</sup> minute of observation. When Rt, Dhq and Tm were administered before the induction of acute pancreatitis, the absorption of glucose from a sucrose was recorded at the control level at the 15<sup>th</sup> and 30<sup>th</sup> minutes of observation. Pl did not have a preventive effect on the absorption of glucose from a sucrose solution in the jejunum segment in experimental pancreatitis. In all groups of rats, the transition of glucose into the blood from a sucrose solution did not depend on the time of incubation of the substrate in the intestine (Figure 3).

The results of the antipancreatic preventive effect of flavonoids on the absorption of glucose from the glucose solution in the small intestine into the blood are shown in figure 4.

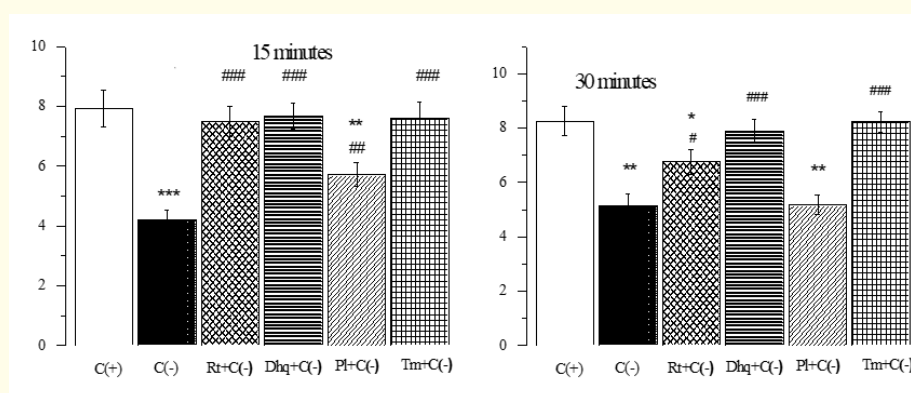
In animals with acute pancreatitis, the decrease in absorption of glucose from the monomer solution was 19.0% in 15 minutes of observation, and 27.7% in 30 minutes. In this case, the preventive anti pancreatitis effect of Rt, DGK and Tm on repression of absorption of glucose from monomer solution in jejunal segment was observed in. Preventive effect of Pl on glucose absorption caused by pancreatitis was not note.



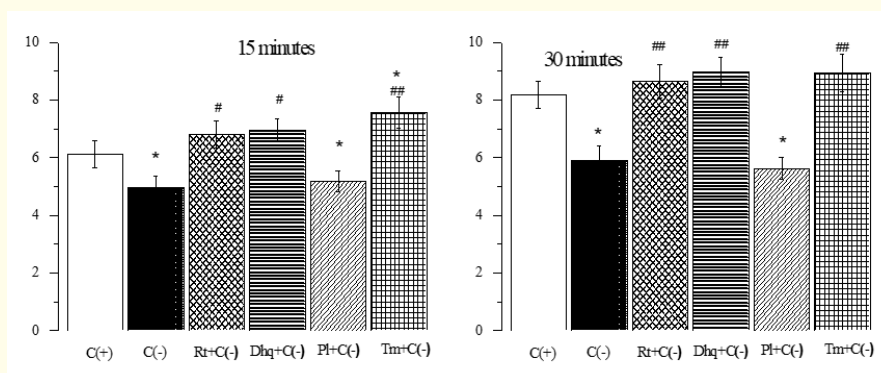
**Figure 1:** Effect of intragastric administration of flavonoids before the induction of L-arginine pancreatitis on the absorption of glucose from the jejunum cavity starch solution into the blood ( $M \pm m$ ;  $n = 6$ ); on the y-axis glucose level (mmol/l); \* -  $<0.05$ ; \*\* -  $<0.01$  compared to positive control (C+), # -  $<0.05$ ; ## -  $<0.01$  compared to negative control (C-)



**Figure 2:** Effect of intragastric administration of flavonoids before the induction of L-arginine pancreatitis on the absorption of glucose from the jejunal maltose solution into the blood ( $M \pm m$ ;  $n = 6$ ); on the y-axis glucose level (mmol/l); \* -  $<0.05$ ; \*\* -  $<0.01$  compared to positive control (C+), # -  $<0.05$ ; ## -  $<0.01$ ; ### -  $<0.01$  compared to negative control (C-)



**Figure 3:** Effect of intragastric administration of flavonoids before the induction of L-arginine pancreatitis on the absorption of glucose from the jejunal sucrose solution into the blood ( $M \pm m$ ;  $n = 6$ ); on the y-axis glucose level (mmol/l); \* -  $<0.05$ ; \*\* -  $<0.01$ ; \*\*\* -  $<0.001$  compared to positive control (C+), # -  $<0.05$ ; ## -  $<0.01$ ; ### -  $<0.001$  compared to negative control (C-).



**Figure 4:** Effect of intragastric administration of flavonoids before the induction of L-arginine pancreatitis on the absorption of glucose from the jejunal glucose solution into the blood ( $M \pm m$ ;  $n = 6$ ); on the y-axis glucose level (mmol/l); \* -  $<0.05$ ; \*\* -  $<0.01$ ; \*\*\* -  $<0.001$  compared to positive control (C+), # -  $<0.05$ ; ## -  $<0.01$  compared to negative control (C-).

Thus, the results showed that in experimental pancreatitis, the absorption of glucose in the small intestine from poly-, oligo and monosaccharides is repressed. However, if rats are treated intragastrically with Rt, Dhq, and Tm flavonoids before disease induction, the decrease in glucose absorption associated with pancreatitis can be prevented.

Perhaps the cause of malnutrition and exhaustion that occurs in pancreatitis is precisely the repression of glucose and possibly other nutrients absorption in the small intestine. This inhibition of glucose transport may be associated with depressing of enteral carbohydrase activity, which occurs in the pancreas disease [7]. Increased sympathetic tone during pancreatitis, which has been noted in clinical practice [8] probably also has contributed in the intestinal glucose absorption. Impaired absorption of nutrients, as our data show, can be prevented by preliminary intragastric administration of Rt and Dhq flavonoids with broad pharmacological properties. Since Tm has not previously been studied as widely as the other flavonoid, additional experimental studies are required for its introduction into practical medicine. Thus, these data show that the range of use of some biologically active additives such as Rt and Dhq can be expanded by adding them to prevent the absorption of glucose, and possibly other nutrients in pancreatitis. The use of Pl and Tm requires additional research.

## Conclusion

The absorption of glucose in the intestine is the final stage of the assimilation of carbohydrates in the small intestine is decreases in pancreatitis notably. Consumption of Rt and Dhq flavonoids, may prevent disease-dependent reductions in glucose transport from carbohydrates substrates. For Rt and Dhq, conducting clinical studies is not difficult, because these drugs have already entered practical medicine as preventive and corrective agents for a wide variety of diseases. The data we obtained only speaks about the possibility of expanding their preventive and possibly corrective agents for glucose absorption in acute pancreatitis. However, additional experiments and clinic observations is required for Pl and Tm.

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