

## THE EFFECTS OF ASCORBIC ACID ON MEMBRANE TRANSPORT OF GLUCOSE

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In this study we compared the effects of ascorbic acid on the glucose levels in the plasma.

At the beginning of the experiment the level of ascorbic acid and the level of glycemia were determined twelve hours after the last meal. In the following seven days each of the examined women was given, beside the usual nourishment, 1000 mg ascorbic acid (two times a day of 500 mg with breakfast and lunch). The level of ascorbic acid and glycemia was determined on the eight day of the experiment, twenty-four hours after the last taken dosage of ascorbic acid. The achieved results of oral glucose  $\ddagger$  tolerance test (OGTT) at the beginning and in the end of the test were shown in a table and on a diagram.

The intake of ascorbic acid in the dosage of 1000 mg/a day for seven days, intensifies the level of glycemia during OGTT.

This hyperglycemia is probably the consequence of receptor obstruction in cellular membrane by ascorbic acid. *Acta Medica Mediana 2004; 43(3): 29-31.*

**Key words:** *ascorbic acid, glycemia, vitamin C*

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### Introduction

In most species, the hepatic metabolism of glucose includes the synthesis of ascorbic acid (1). In man, monkey and guinea pigs, however, the absence of one enzyme in that pathway (2) necessitates the dietary intake of a micronutrient, termed „antiscorbutic chemical’’ in citrus fruits was well appreciated long before Szent-Georgi’s (3) isolation of ascorbic acid itself in 1928.

In particular, the cellular uptake of ascorbic acid is regulated by both glucose and insulin and the renal reabsorption of ascorbic acid is impaired by hyperglycemia (4). Evidence also suggests that vitamin C supplementation may be beneficial in countering the pathophysiologies resulting from the chronic hyperglycemia of insulin-dependent diabetes mellitus (IDDM).

Levels of ascorbic acid decrease in various tissues of animals with experimental diabetes (5). Mann suggested (6) in 1974 that glucose and vitamin C might occupy the same membrane transport system. He subsequently reported with Newton (7) that elevated glucose levels interfered with cellular ascorbic

acid was transported in erythrocytes. Others have observed inhibition by glucose of ascorbic acid in vitro by human lymphocytes (8) and bovine endothelial cells (9). Bigley et al. (10) described competitive inhibition between the in vitro uptake of dehydroascorbic acid and glucose analogues by human polymorphonuclear leukocytes (PMN) and fibroblasts, and concluded on the basis of kinetic data that the competing ligands utilized the same membrane carrier.

In this study we compared the effects of ascorbic acid on the glucose levels in the plasma.

### Materials and methods

During 2002, the level of glycemia and ascorbic acid was tested on Gynecology clinic in Nis. This test was done on thirty healthy normoglycemic adult women, aged 18 and 30, having no clinical signs of endocrine disturbances.

At the beginning of the experiment the level of ascorbic acid and the level of glycemia were determined twelve hours after the last meal. In the following seven days each of the examined women was given, beside the usual nourishment, 1000 mg of ascorbic acid (two times a day of 500 mg with breakfast and lunch). The level of ascorbic acid and glycemia was determined on the eight day of the experiment, twenty-four hours after the last taken dosage of ascorbic acid. The achieved results of oral glucose-tolerance test (OGTT) at the beginning and in the end of the test were shown in a table and on a diagram.

## The results

In the case of thirty normoglycemic adult women, aged 18 and 30, the oral glucose tolerance test was done with 75g of glucose. The achieved values of glycemia were shown in Table 1.

Table 1. The values of glycemia during OGTT (mmol/L) at the beginning of the experiment

Time (min)	0	30	60	90	120
glucochemy	3.77	6.82	7.93	7.04	4.1

After OGTT had been, and after having taken 1000 mg of ascorbic acid every day, the oral glucose-tolerance test was determined. The achieved values were given in Table 2.

Table 2. The values of glycemia during OGTT (mmol/L) in the end of the experiment

Time (min)	0	30	60	90	120
glucochemy	4.16	9.1	10.71	9.04	6.82

The above given results show the existence of the level of glycemia in the case of all examined normoglycemic adult women, after taking 1g of ascorbic acid during the period of seven days. This difference is more obvious when presented by the following Diagram 1.

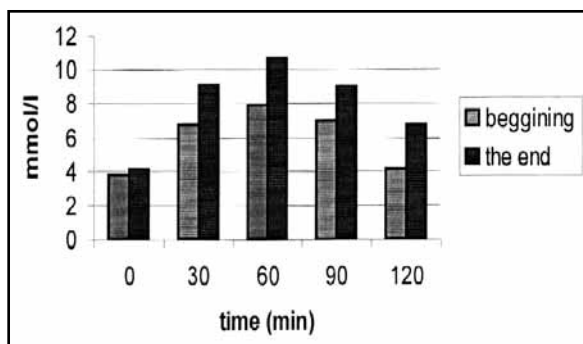


Diagram 1. The values of glycemia during OGTT (mmol/L) at the beginning and at the end of the experiment

Namely, the level of glycemia, after applying ascorbic acid is higher in all the intervals of determining of oral glucose tolerance test (OGTT). These differences are more important statistically ( $p < 0,001$ ).

## Discussion

In most species, the hepatic metabolism of glucose includes the synthesis of ascorbic acid. Glucose has a similar structure, and is the precursor for the vitamin in species which synthesize it (11). Although the biosynthetic relationship between glucose and vitamin C is absent in man. On the basis of in vitro examination of tissue homogenate extracts Burns (2) concluded that, man, monkey and guinea pig were unable to convert L-gulonolactone to L-ascorbic acid, and that this was the „missing step“ in the biosynthe-

sis in the livers of these species which made them dependent on exogenous ascorbic acid for their vitamin C requirements. Chattered et al. (12) concluded that there existed an additional „missing step“, namely performed in other species by the enzyme L-gulonolactone oxidase in converting D-gulonolactone to L-gulonolactone. More specifically Burns (2), Stone (13) and Chattered et al. (12) considered that the „missing step“ was due to gene deletion.

In his seminal paper „Evolution and the Need for Ascorbic Acid“ Linus Pauling (14) concluded that the loss of the ability to synthesize ascorbic acid had probably occurred in the common ancestor of the primates. A rough estimate of the time at which this mutational change occurred was twenty-five million years ago.

Weighty experimental and theoretical considerations will advance in favour of the thesis that vitamin C deficiency in a number of species including humans is not due to total inability to biosynthesize ascorbate, but rather to a very limited biosynthetic ability which normally cannot be stopped to meet minimal metabolic /physiological requirements (15, 16,17,18).

The cellular uptake of ascorbic acid from plasma can occur by two mechanisms. An active transport of ascorbic acid is documented (4, 19). With regard to this active transport, insulin has been shown to accelerate ascorbic acid clearance from plasma, and presumably into cells since there is no increase in urinary excretion (20, 21).

Hyperglycemia has turned out to inhibit ascorbic acid transport. This inhibition seems somewhat paradoxical since the given evidence suggest that insulin promotes both ascorbic acid and dehydroascorbic acid (DHA) uptake by cells. The inhibition of ascorbic acid uptake by hyperglycemia was demonstrated in vitro in the absence of insulin and may not, therefore, be important in normal physiology. Hyperglycemia is also known to enhance renal ascorbic acid losses (4, 20, 23).

The glucose transport system also transports the minor oxidized and uncharged species, DHA with a presumed subsequent intracellular reduction to ascorbic acid. Cunningham (24) showed that DHA competes for glucose transport system transported on an equimolar basis with the transport surrogates 2-deoxyglucose and 3-o-methyl glucose. Earlier studies (10) clearly show an enhancement of leucocyte DHA uptake by insulin, consistent with the requirement of glucose transport system transporters from the cytosol to membrane surfaces. Much emphasis has been placed on this potential uptake mechanism (24).

## Conclusion

The results of this experiments doliged us to conclude:

The intake of ascorbic acid in the dosage of 1000 mg/a day for seven days, intensifies the level of glycemia during OGTT.

This hyperglycemia is probably the consequence of the receptor obstruction in cellular membrane by ascorbic acid.

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## UTICAJ PERORALNOG UNOSA ASKORBINSKE KISELINE NA NIVO GLIKEMIJE KOD ZDRAVIH OSOBA

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U medicinskoj literaturi postoje mnogobrojni podaci o efektima askorbinske kiseline na pojedine aktivnosti organizma. Me|utim, relativno mali broj radova obra|uje problem efekata askorbinske kiseline na nivo glikemije i sistem glikoregulacije.

Izu-avan je uticaj askorbinske kiseline na nivo glikemije kod 30 zdravih, normoglikemi-nih `ena, starosti izme|u 18 i 30 godina, koje nisu imale klini-ke simptome nekog endokrinog poreme}aja. Kod svih ispitanica ura|en je oralni glikozo-tolerans test (OGTT) sa 75 g glikoze, na po-etku ogleada. Narednih sedam dana, svaka ispitanica, per os, unosila je po 1000 mg askorbinske kiseline na dan. Osmog dana (24 h posle poslednje doze unete askorbinske kiseline), kod svake ispitanice, ura|en je OGTT. Dobijeni rezultati pokazuju da postoji zna-ajna razlika u nivou glikemije, pre i posle uzimanja askorbinske kiseline. Posle sedmodnevnog uzimanja askorbinske kiseline nivo glikemije je zna-ajno vi{i, du`e traje i sporije se vra}a na po-etnu vrednost. Ova razlika u nivou glikemije, mogla bi biti posledica kompetitivnog delovanja askorbinske kiseline i glikoze na zajedni-ke receptore transportnog mehanizma u celularnim membranama. *Acta Medica Medianae* 2004; 43(3): 29-31.

**Klju-ne re-i:** askorbinska kiselina, glikemija, vitamin C