Glucose and inulin: Caenorhabditis elegans a model of diabetes

Abstract
Carbohydrate levels in the diet are important in a wide variety of living organisms, due to essential requirements such as the production and use of energy to meet the basic demands of cellular functioning. However, the high supply of glucose carbohydrate is a risk factor in the development and maintenance of metabolic disorders such as diabetes; in addition, to be closely related to the excessive production of radioactive oxygen species (EROs), which generate loss of redox balance, direct cellular damage, involvement of the critical component of the aging process, initiation and development of diseases of notable morbidity and mortality (atherosclerosis, cancer, diseases of the central nervous system, autoimmune diseases, ischemia-reperfusion injury) among others. Caenorhabditis elegans is an adequate model in a wide variety of studies. Some studies suggest that the increase in glucose metabolism decreases the half-life of C. elegans, so it has become a model of studies of oxidative stress that can be produced in diabetes mellitus.

Keywords: glucose, inulin, caenorhabditis elegans, oxidative stress

Introduction
Currently, the hyperglycemic state has marked an important point as the existence of diabetes, which stands out for its increased incidence and is characterized as a global disorder in the body which includes alterations in carbohydrates, lipids and proteins. Diabetes is classified as a metabolic disease in which there is an imbalance in glucose levels. Diabetes mellitus leads to increased ROS and a reduction in antioxidant defenses, increasing the oxidative stress responsible for many of the complications of this disease. Free radicals are capable of causing damage in different tissues and contribute to the establishment of late complications of diabetes.

The direct relationship between oxidative stress and diabetes mellitus is an interesting topic of study, due to the presence of free radicals that have also been reported in patients diagnosed with pathologies such as Parkinson’s disease. In order to allow the inclusion of diabetes within the diseases caused by oxidative stress, it is necessary to experimentally and theoretically verify the established criteria to associate them in a significant way. In diabetics, a greater production of ROS has been found and weakening of the antioxidant defenses responsible for the elimination of free radicals.

Glucose e inulin
Glucose is the most abundant monosaccharide in nature and essential for life, it is the primary source for the synthesis of energy at the cellular level through its oxidation and catabolism. It is the initial component or the result of the main carbohydrate metabolism routes and together with fructose and galactose is absorbed and taken directly into the bloodstream. Glucose is an essential carbohydrate for most organisms, since it provides one of the main sources of energy. On the other hand, it has been documented that other carbohydrates such as inulin do not generate toxic effects in humans similar to those produced by glucose in high quantities.

On the other hand, inulin is a food that provides a lot of fiber, and compared to other carbohydrates such as glucose, its caloric content is lower. Inulin is a non-digestible carbohydrate, is present in various fruits, vegetables, cereals and more than 36,000 species of plants worldwide; It can be used as an ingredient in functional foods, due to being described as a nutrient with beneficial selective activity, which confers a physiological effect in addition to its nutritional value. Inulin is constituted by fructose molecules linked by β-(2→1) fructosyl fructose bonds. Given its chemical conformation, inulin is not hydrolyzed by human digestive enzymes, which means that it remains intact during its passage through the upper part of the gastrointestinal tract. However, inulin is fermented and hydrolyzed in its entirety by the bacteria present in the large intestine.

Reactive oxygen species and diabetes
The importance of reactive oxygen species in various pathologies has been proposed in order to achieve closer approaches to the real causes and possible treatments of diabetes mellitus. A report made in 2013 by Calderón et al. proposes theoretically the relationship between the increase of reactive oxygen species and diabetes mellitus. However, in order to classify a disease as a secondary cause of the increase in EROs, it is necessary to comply with parameters such as the presence of radicals at the specific site of development of the pathology; show a direct relationship between the pathology and the production of radicals, as well as the reduction or elimination of the condition when executing an antioxidant therapy or removing the free radicals that cause the condition.

Although the influence of EROs on diabetes mellitus has not yet been confirmed with certainty, the existence of a state of oxidative stress has been documented in frequent complications of Diabetes mellitus such as diabetic retinopathy, the main cause of vision loss...
in patients with diabetes diabetic people. The imbalance between the production of EROs and the antioxidant defense system activates several oxidative mechanisms that are related to stress and are the cause of diabetic retinopathy.\(^9\)

**Caenorhabditis elegans xidative stress model**

*C. elegans* turns out to be an adequate model in a variety of studies due to characteristics such as its easy handling at the laboratory level or its great homology with human genes. Studies with *C. elegans* in cultures rich with glucose have been able to demonstrate the significant reduction of the half-life in the wild strain (N2) mediated by inhibition of transcription factors or mechanisms other than the reduction and inhibition of respiration in the nematode.\(^1\) Together with these studies, the effect of glucose on *C. elegans* crops has been determined and its close relationship with the increase in the production of triglycerides and fatty derivatives, which would lead to a significant decrease in the half-life in the strain wild.\(^9\)

Tests in the model, propose the production of EROs by increasing the amount of glucose in the nematode culture, a decrease in the half-life of the nematode has been observed by promoting the increase of oxidative metabolism at the mitochondrial level.\(^1\) Many studies have addressed the effect of diet on the glycemic index, obesity and diabetes, but little is known about the mechanisms that affect the life expectancy of the nematode. However, some studies have shown that glucose shortens lifespan by inhibiting the activity of transcription factors, which play an important role in maintaining the life expectancy of the nematode.\(^1\)

Interestingly, the male - hermaphroditic differentiation in the nematode has presented marked points in its anatomy, nervous system and behavior in adulthood. The differences in the sex of *C. elegans* is marked mainly by the activation of genes, in which it is possible to observe that the gene pathways of glycolysis are highly expressed in the male, unlike the hermaphrodite, with differences of sex in the metabolism. Of carbohydrates linked to gene expression, which would lead to different effects subsequent to the synthesis and metabolism of carbohydrates.\(^10\)

On the other hand, the analysis of reproduction in *C. elegans* is often done because it is considered a species with a reproduction rate that shows a physiologically strong phenotype maintained by transgenerational inheritance. Tauffenberger Arnaud et all carried out a study in 2014 in which they cultured the strain N2 in medium supplemented with glucose, they were able to verify the reduction in the reproductive levels but even inducing a hereditary phenotype; that is, the same significant reduction in the reproduction rate was found in the progeny, both in the F1 generation and in the second generation (F2) with only one exposure of the parental line.\(^11\)

As documented in several studies, the increase in glucose concentrations in *C. elegans* cultures has a negative effect on reproduction and survival rate; even so, a strong increase in the capacity of resistance to oxidative stress after exposure with glucose has been reported.\(^12\)

To test this resistance, the N2 strain was subjected to concentrations of 4% glucose, after which a culture was performed in which the strain was exposed to a natural product (Juglone) that produces increased oxidative stress at the intracellular level and later to this the decrease of the survival of the nematode. It was found that the previous treatment with glucose gave a strong protective effect against the increase of oxidative stress, being transmitted to the first generation (F1) without this having had contact with glucose.\(^13\)

This is how the cultivation of *C. elegans* with increased glucose concentrations (0.2–2%) means a significant increase in glucose levels (greater than 50%) compared to nematode cultures under normal conditions. These studies confirm the direct relationship between the administration of glucose to *C. elegans* and the reduction in the half-life, which is a factor that enhances aging and shortens the “useful” life of the nematode.

### Conclusion

Finally, caloric restriction studies that have been studied in all species are interesting. Extension of lifespan results from decreased signaling through the insulin/insulin-like growth factor (IIS) signaling pathway. An effective method to combat the damage of free radicals occurs through the metabolism of ketone bodies, products of fat metabolism. They occur when the body uses fats instead of sugars to generate energy. Ketosis results in the transcription of antioxidant pathway enzymes, Veech RL in 2017 suggest that increased levels of ketone bodies also extend life in the C elegans model as well as caloric restriction. They suggest new lines of research for preventive measures and treatments for disorders studied with this model.

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### Conflict of interest

Authors declare that there is no conflict of interest.

### References

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