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Abscisic acid: A mean of Glycemic homeostasis.

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ABSTRACT

Abscisic Acid has lately emerged as one of the primary contenders to tackle diabetes and maintain glycemic conditions appropriate for the body. It is a plant hormone but is also found in other organisms like Metazoans. Dietary intake of abscisic acid results in abscisic acid being present in humans. However, some claim that ABA might be produced inside humans itself. Abscisic acid plays an important role in managing our internal environment. Moreover, recent studies have found that it binds to a receptor called Lanthionine synthetase C-like 2 which further helps the facilitated diffusion of glucose molecules into cells. Vitamin D is also directly responsible for ABA functioning and maintaining homeostasis. This review has been formulated based on accounts and research papers of people who have done in depth analysis on the topic. It summarizes the functioning and origin of abscisic acid and how it can be used as a way of controlling glucose concentration in the blood. It also aims to provide a scalable solution to a common metabolic disorder that is diabetes.

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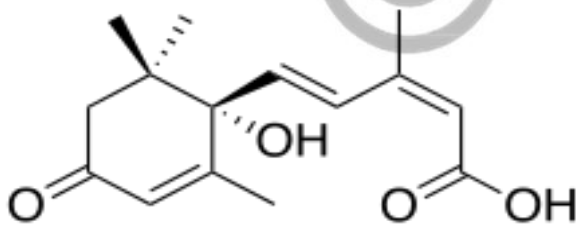
1. INTRODUCTION



Abscisic acid was discovered 50 years ago by F.T. Addicott and his associates in the early 1960s in the process of studying abscission in cotton. ABA is a weak acid with the chemical formula $C_{15}O_{20}H_4$ and is usually associated with major plant responses to stress. It is a single compound unlike the auxins, gibberellins, and cytokinins. It was called "abscisin II" originally because it was thought to play a major role in abscission of fruits. At about the same time another group was calling it "dormin" because they thought it had a major role in bud dormancy. The name abscisic acid (ABA) was coined by a compromise between the two groups.

Abscisic acid (ABA) is often referred to as a inhibitory hormone rather than stimulatory hormone. Over the years, many studies have been done on ABA and it is found to be a very important hormone in not only plants but fungi and animals too.

1.1. ABA in Plants.

ABA is a very important plant hormone that performs various functions. Plants mainly accumulate ABA and activate it when there is a stress stimulus like drought. One of the major functions of ABA is to control the closure of the stomata. Large quantities of the acid gather when the plant has to close its stoma in order to conserve water during droughts. Various conditions are also mediated by ABA such as excess ultraviolet-B light, temperature variants, and nutrient availability. Abscisic acid is produced in the roots of the plant as well as the terminal buds at the top of the plant.

1.2. ABA in Lower Metazoans.

ABA is found at lower metazoan levels. It plays similar role to the role it has in plants which is to regulate stress conditions and variations in the environment. ABA is found in sponges and inhibits and commands other hormones to react to stimuli such as temperature changes in the water.

1.3. ABA in mammals.

ABA is also found in one of the most complex class of organisms which is the mammals. However, it has varying functions in different mammals which will be further discussed in the review. ABA was first found to be present in mammals in the central nervous system of pigs and rats. The presence of abscisic acid conjugates the one that are present in plants. The fact that mice have a very similar set of genes to humans encouraged many people to check for the presence of abscisic acid in humans. In fact, according to National Human Genome Research Institute, humans and mice in 4,000 genes have less than 10 which are unique and different from one another. This laid the foundation for many researchers to read and study about Abscisic acid.

1.4. ABA Function and Process in Mammals.

ABA levels increase whenever there is a high amount of glucose concentration in the blood. There are claims that this is due to the fact that beta cells **β** are responsible for the production of ABA along with insulin. Although ABA is not directly related or associated with insulin it indirectly helps insulin functioning. Oral glucose load stimulates insulin release from pancreatic β-cells principally *via* the incretin GLP-1, which is believed to account for up to 70% of glucose-stimulated insulin release . GLP-1 is produced and released into the blood by enteroendocrine cells (L cells) in response to high glucose concentrations in the gut. ABA induces glucose-independent GLP-1 release in the human L cell line hNCI-H716 through a cAMP/PKA-dependent mechanism and also enhances GLP-1 transcription. This shows that ABA is also responsible for insulin secretion and is very important. In response to high levels of glucose, ABA looks for lanthionine synthetase-C like protein, abbreviated LANCL receptors which are present on fat cells. This attracts attention of Akt2 which continues the process. This is a very important process in the human body as after attracting attention of Akt is only when can glucose be translocated.

1.5. The mammalian receptor for ABA – LANCL 2.

Several evidences show that Lanthionine synthetase C-like 2 is the mammalian receptor for ABA. A study conducted by scientists proved that LANCL 2 is required for binding to ABA. Affinity chromatography was done on immobilized ABA showed binding proving that LANCL 2 is the main receptor. The ABA-LANCL 2 binding has high KD and less affinity but the bonding is still strong enough to stimulate a reaction. The binding also stimulates signaling in 4 different types of liver cells granulocytes, HeLa cells, and RIN-m and INS-1 cells). In human granulocytes Ca2+ ions re-released as a result of ABA binding with LANCL 2 and this causes functional insulin release too sometimes. ABA and LANCL 2 binding are a very crucial process for glucose homeostasis. In response to high levels of glucose, ABA looks for lanthionine synthetase-C like protein, abbreviated LANCL receptors which are present on fat cells. When abscisic acid starts jiggling on LANCL, it attracts the attention of Akt2. AKT2 sends the glucose deliveries. Akt2 is required for the insulin-induced translocation of glucose transporter 4 (GLUT 4) to the plasma membrane

At the cell surface, GLUT4 permits the facilitated diffusion of circulating glucose down its concentration gradient into muscle and fat cells. Once within cells, glucose is rapidly phosphorylated by glucokinase in the liver and hexokinase in other tissues to form glucose-6-phosphate, which then enters glycolysis or is polymerized into glycogen. Glucose-6-phosphate cannot diffuse back out of cells, which also serves to maintain the concentration gradient for glucose to passively enter cells.

1.6. ABA as a dietary source.

In the human body, ABA naturally originates from dietary sources and endogenous production through the carotenoid biogenesis pathway. However there are disputes made and recent evidence has shown that ABA is also endogenously produced. But it is important that consumption of fruits like avocados which contain high concentration of ABA is not reduced as claims are made that the amino acids gained by consumption are responsible for the production.

According to research made by Elena Zocchi, on average the concentration of ABA is 0.29/mg/kg wet weight of vegetable and 0.62 mg/kg of wet weight of fruit. The current recommendation is to eat ≥4.5 servings/day, which would lead to ≥297 µg of ABA per day in an ideal situation. So in India the average intake of fruits and vegetables is 4 servings a day which is very close to the 4.5 serving average of fruits and vegetables required. Thus although diabetes is quite high in India it is important to know that rate has gone down since the past years and these high number of cases can be misleading as the population of India is very high itself.

1.7. Vitamin D and ABA connection

ABA and Vitamin D are related. There have been recent studies that have shown Vitamin D Regular doses of vitamin D —about 2000 IU/d—early in life have been shown to reduce the risk of developing type 1 diabetes (up to an 80% reduction projected over the next 30 years). This is very interesting as it should be noted that ABA is produced by beta cells and plays a role in glucose homeostasis. Calcium two plus ions has been shown to be produced in the cytosol after ABA and LANCL2 binding .However the formation of calcium ions could be due to calcium playing a role in the binding of ABA and its receptor. This could lead to calcium getting ionised and thus an increase in cytosolic Ca+2 concentration.

Vitamin D is directly responsible for Calcium absorption and thus an increase in vitamin D reduces diabetic risk. Dietary consumption of Vitamin D and exposure to sunlight leads to more ABA binding and leads to glucose levels decreasing in blood when needed. Vitamin D is crucial for fatty acid oxidation as well and this reduces obesity which is also a major contributing factor for diabetes. Your skin hosts a type of cholesterol that functions as a precursor to vitamin D. When this compound is exposed to UV-B radiation from the sun, it becomes vitamin D. Recently people have started intaking vitamin d tablets and calcium is now mandatory in mineral water. These dietary changes will help maintain a good control over metabolism.

2. Conclusion

All in all, metabolic disorders are very serious now a days and proper care needs to be taken as we still haven't come up with a 100% effective solution. However, the signs are promising for ABA being used and Vitamin intake right now in the early stages. Yet, more research and experiments will need to be done on the topics so that we have a clearer idea of the functioning and relation between ABA and LANCL 2 and Vitamin D. It is advisory to increase Vitamin D intake and Calcium intake by prediabetic patients and also to have dietary consumption of ABA.

Acknowledgement

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