Analele Universităţii din Craiova, seria Agricultură – Montanologie – Cadastru (Annals of the University of Craiova - Agriculture, Montanology, Cadastre Series) Vol. 54/1/2024

GENOME-EDITED FOODS AVAILABLE ON THE MARKET

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Abstract

New genomic techniques (NGT), especially CRISPR/Cas9 (molecular scissors) are increasingly used in the food industry. The first genome-edited foods are already on the market of several countries where these products do not require specific approvals, being classified as non-GMO products (without foreign DNA).This review summarizes the first genome-edited foods that have been commercialized or approved but not yet commercialized in some countries, their advantages, as well as the current international legislation regarding their regulation. Awareness of the advantages of NGT and the credibility of the information is essential in consumer acceptance and widespread expansion of genome-edited foods.

***Key words**: CRISPR, products commercialization, New Genomic Techniques (NGT), TALEN.*

INTRODUCTION

The long time required to obtain new improved varieties using traditional breeding methods has led researchers to explore alternative breeding approaches, such as transgenic technology.

Unlike traditional approaches, transgenesis allows the modification of the genetic information of a plant cell, obtaining a new genetically modified organism (GMO) or transgenic that has a foreign DNA fragment in its genome that gives it a new trait (Permyakova et al., 2024).

The first transgenic food that came to the attention of the US public was the *FlavrSavr*™ tomato (delayed ripening) obtained in 1994. Since their first commercialization, transgenic products have developed rapidly, changing agriculture and food production in many countries. For example, in 1996, genetically modified crops were cultivated on 1.7 million hectares, and in 2019 they reached 190.4 million hectares (Bonea, 2023).

Despite considerable efforts by various countries, many results of this transgenic research could not be used due to regulatory restrictions and public concerns about the safety of genetically modified (GM) foods (Bonea, 2024; Zhang et al., 2024).

The advent of new genomic techniques (NGT), especially the CRISPR/Cas9 technique, has significantly alleviated public concerns about the introduction of foreign genes into food. By using this precision editing technique, foods can be rapidly developed to meet consumer expectations and requirements without fear of incorporating foreign genes. Currently, genome editing technology has a wide range of potential applications both for agricultural crops by improving crop yields, their nutritional value and environmental impact, and for farm animals by improving animal production traits, health and of their well-being (Gao et al., 2023). As a result, genome editing offers hope for combating global food insecurity and malnutrition.

Cereals contribute approximately 50% of food energy globally (WHO/FAO, 2003). Legumes are nutritionally valuable, providing complex carbohydrates (±60%), protein (20-45%) and dietary fiber (5-37%) (Maphosa and Jideani, 2017; Soare et al., 2018). Also, farm animals provide proteins and animal fats necessary for people's daily life (Colă and Colă, 2017; 2019).

The start of the commercialization of genome-edited products has led to the adoption of regulatory frameworks that differ globally, from non-existent to equivalent to those applied to genetically modified organisms, which can even be considered a ban on new genomic techniques (Smyth et al., 2022).

According to Tachikawa and Matsuo (2023), at the global level there seems to be a tendency especially towards the adoption of two approaches regarding the regulation of genome-edited products, namely: one that considers them GMOs, but tries to apply simplified regulations (Australia, New Zealand, China, UK), and one that exempts them from GMO regulations but requires government confirmation before placing on the market (Argentina, Chile, Israel, Brazil, Japan, Canada, India, Philippines). In the US these genome-edited products are exempt from GMO regulations. In the European Union, genome edited products are still subject to GMO regulation as in New Zealand.

In July 2023, the European Commission proposed a relaxation of the GMO rules regarding plants in the NGT1 category (to be considered equivalent to conventional products), a proposal that the European Parliament approved in February 2024 (EU, 2024), thus opening the way for negotiations with the Council, but the whole process, from negotiating the proposal to adopting new legislation, can take between 18 months and two years (Polidoros et al., 2024).

MATERIALS AND METHODS

Data on NGT applications were collected from the Global Gene Editing Regulation Tracker (GGERT), National Institutes of Health (NIH), International Service for the Acquisition of Agri-biotech Applications (ISAAA) and other online sources.

This review summarizes some of the first genome-edited foods that have been commercialized or approved but not yet commercialized in some countries.

RESULTS AND DISCUSSIONS

Few genome-edited foods are approved and commercialized, and many innovations await commercial approval or are in development. The initial commercialized traits aimed at increasing the nutritional value, changing the composition of the oil, improving the shelf life, in order to satisfy the demands of consumers and the industry (Polidoros et al., 2024).

Calyno™ Soybean Oil

Calyno™ Soybean Oil obtained by Calyxt Company Inc. (USA) through the TALEN technique for knocking out the fatty acid desaturase genes *FAD2-1A* and *FAD2-1B,* being the first genome-edited food product commercialized in the USA since 2019 and promoted as a non-GMO product (GGERT, 2024).

This type of oil has health benefits due to a high oleic acid content of about 80% and a lower linoleic acid content of about 5% compared to the classic oil that contains about 20% oleic acid and 50% linoleic acid (ISAAA, 2019).

High oleic soybeans (Figure 1) are an alternative to partially hydrogenated soybean oil, providing an oil free of trans fatty acids and more shelf-stable than conventional soybean oil.

Fig. 1. Calyno Soybean Oil
Source: GM Watch, 2021

Waxy maize with a high-starch amylopectin

The company Corteva Agriscience has developed waxy maize with a high starch content required for the food industry where it is used as a thickener and stabilizer, but also for other industries (for example, the textile and paper industries), using the CRISPR/Cas9 technique (Gao et al., 2020). Through this technique, a targeted deletion of the *Waxy* gene (*Wx1*) was achieved, thus increasing the amylopectin content of starch to almost 100%. In conventional maize, starch is generally composed of 75% amylopectin and 25% amylose.

In 2020, Canada announced that "CRISPR-Cas waxy maize" is considered safe for use (Chilcoat, 2020; USDA, 2023). The governments of the US, Brazil, Argentina and Chile have also authorized Waxy maize for release. The latest approval for the commercialization of this product was in 2024 in Japan (GGERT, 2024).

High GABA tomato

Sanatech Seed Co., Ltd., together with Pioneer EcoScience Co, Ltd., have developed a genome-edited tomato variety called "Sicilian Rouge High GABA" that contains five to six times more GABA (gamma-aminobutyric acid) than conventional tomatoes. This product was developed using the CRISPR/cas9 technique to increase the content of GABA (Nonaka et al., 2017). In 2021, Japan approved this variety for commercialization (ISAAA, 2021; 2022c).

Several previous studies have shown that GABA is an amino acid that has beneficial effects on insomnia, stress and blood pressure (Guertler et al., 2023).

Therefore, daily intake of GABA-enriched foods would be an effective way to prevent these diseases.

Purple tomato

Purple tomato developed by Norfolk Healthy Produce, Ltd. was approved by USDA/APHIS in 2022 for import and cultivation in the US (ISAAA, 2022a; 2023a).

This was obtained by applying the CRISPR technique and contains a large amount of anthocyanins, compounds that give it its purple color (Figure 2). Anthocyanins are natural plant compounds that act mainly as antioxidants, diets rich in anthocyanins offer many health benefits, namely anti-inflammatory, anti-carcinogenic, anti-microbial and anti-obesity effects (Smeriglio et al., 2016).

Fig. 2. Purple tomato
Source: NORFOLK, 2024

Cibus' herbicide-resistant canola

The widespread use of chemical pesticides has a devastating impact on the ecosystem of soil, water and people (Bălan and Popescu, 2024; Bălan et al., 2024; Popescu and Bălan, 2024; Popescu et al., 2024).

Herbicide-tolerant varieties offer farmers a technical answer to weed control, their use meaning less herbicides released into the environment or the use of less harmful herbicides.

Cibus' herbicide-resistant canola was developed by the Cibus Company. Inc (USA) and is considered to be the first variety obtained through NGT and approved for sale in Canada and the USA since 2013 and 2014, respectively (Guertler et al., 2023; GGERT, 2024).

It was obtained by Oligo-Directed Mutagenesis (ODM) - mediated genomic editing in canola (Gocal et al., 2015) and possesses a specific single nucleotide mutation in the *BnAHAS1C* and *BnAHAS3A* genes, which confers increased tolerance to imidazolinone and sulfonylurea herbicides.

Development and cultivation of herbicide tolerant crops is very important in reducing weed infestations and maintaining sustainable production.

Non-browning banana

Non-browning bananas were developed by UK-based agricultural biotechnology company Tropic Biosciences using the CRISPR/Cas9 technique.

Bananas are known to begin to brown when exposed to oxygen, thus reducing their nutritional quality and market value. Therefore, non-browning bananas obtained by eliminating the function of the enzyme that facilitates this reaction can stay yellow longer, thus reducing food waste and CO_2 emissions.

This type of banana was the first genome edited product to go through the regulatory process on genome editing in the Philippines, in 2023 (ISAAA, 2023b; Dionglay, 2024).

Non-browning apple

The non-browning Arctic Apple variety, developed by Okanagan Specialty Fruits Inc. using RNA interference to reduce the enzyme polyphenol oxidase (*PPO*) to less than 10% of what would be found in a regular apple. By suppressing *PPO* production, Arctic apples age and brown at a slower rate - taking three weeks to fully oxidize.

The first Arctic apple cultivars, namely Arctic Golden Delicious and Arctic Granny Smith received regulatory approval in 2015 from the USDA and FDA in the USA and CFIA and HC in Canada (USDA, 2015), and Arctic Fuji was approved for sale in 2016 by APHIS (USA) and in 2018 by CFIA and HC (Canada).

Subsequently, the Arctic Gala variety was approved by the USDA in 2021, and in 2023, the USDA approved another variety for commercial production, namely Arctic Honey (GGERT, 2024).

Lettuce with increased shelf life

Lettuce is one of the most consumed "ready-to-eat" leafy vegetables in the US and the world. However, cut lettuces are perishable producing significant losses due to browning of the cut surface during storage and distribution.

Among the plant enzymes responsible for browning is polyphenol oxidase (*PPO*), which contributes to wound-induced browning in most fruits and vegetables.

Through CRISPR/Cas mediated genome editing, GreenVenus LLC., Precigen Inc. obtained a lettuce plant comprising a mutation in each of at least two different *PPO* genes, wherein said mutations reduce PPO protein activity compared to a lettuce plant wild type. The PPO mutations described here confer multiple beneficial phenotypes to the lettuce plant at harvest and several days after harvest. These phenotypes include, without limitation, reduced browning, reduced tip burn, increased shelf life, increased polyphenol levels increased vitamins, etc (LENS.ORG., 2023).

This genome-edited product was approved for sale in the US in 2024 (GGERT, 2024).

Red Seabream and Fast growing pufferfish

In October and November 2021, two genome-edited fish were approved for commercialization in Japan, namely "*Madai*" Red Seabream and "*22-seiki fugu"* Tiger Puffer (ISAAA, 2022b; 2022c; GGERT, 2024).

Red Seabream is a fish highly appreciated by the Japanese, being considered the "king of fish".

Kyoto University and Kinki University together with the Regional Fish Co., Ltd. used the CRISPR/Cas9 technique to eliminate the gene for the production of myostatin (*Pm-mstn*), which suppresses muscle growth.

Thus they obtained Red Seabream (Figure 3) with 20-60% more edible meat and about 14% more efficient in converting food into edible body mass (Pat, 2023).

Fig.3. Red Seabream
Source: ISAAA, 2022b

Using the CRISPR technique, he same research institutes were able to delete four leptin receptor genes that control the appetite of the puffer fish, thereby stimulating its appetite and weight gain. This genome-edited Tiger Pufferfish (Figure 4) grows faster and is 1.9 times heavier than conventional pufferfish (Shimbun, 2021).

Fig. 4. Tiger Puffer
Source: Shimbun, 2021

CONCLUSIONS

Genome editing enables the deliberate integration of desired genetic characteristics into food through rapid, precise and efficient procedures, thus contributing to building a sustainable and stable food system.

The use of new genomic techniques, especially those that do not incorporate foreign DNA into the host cell, can change consumer perception and increase food security strategies.

Currently, the regulation of genome- edited foods at the international level is characterized by a lack of stability, therefore there is a need for a review, a harmonization and an increase in the degree of consumer awareness.

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