Research Progress on Non-Thermophysical Fresh Keeping Technology of Fruits and Vegetables Based on Nutrition and Safety

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Introduction

Fruits and vegetables are widely loved by consumers because of their rich nutritional value and physiological effects. But harvested fruits and vegetables are still living organisms, carrying out necessary physiological metabolic processes. Moreover, affected by the environment and the nutrition and moisture of fruits and vegetables, post-harvest rot, quality deterioration, and microbial infection are easy to occur (Pinela and Ferreira, 2017; Nxumalo et al., 2021). According to the latest statistics from the food and agriculture organization of the United Nations (http://www.fao.org) (Fig. 1), global vegetable and fruit production rank fifth and seventh respectively. According to the annual data of the national bureau of statistics (https://data.stats.gov.cn), the total domestic output of vegetables and fruits in 2020 reached 749.129 and 286.9236 m tons in China respectively. According to the report of the 2018 China vegetable and fruit physical preservation and industrial chain value enhancement seminar, the fruit loss rate in developed countries is between 3-5%, while the postharvest fruit loss rate in China is as high as 20%, which seriously affects the economic value of fruits. Therefore, how to prolong

Abstract: With the rapid development of the economy and the improvement of living standards, people not only have an increasing demand for fresh fruits and vegetables but also have become increasingly strict on the nutrition, safety, and quality of fruits and vegetables. However, the characteristics of high nutrition and high moisture make them easily susceptible to microbial infection, which can seriously reduce their nutritional value and economic value and even cause food safety problems. Therefore, from the perspective of nutrition and safety, this study examines the application and research of non-thermal physical preservation technologies, such as packaging, irradiation, and cold plasma, in the postharvest storage of fruits and vegetables, and forecasts the research and development trends of fruit preservation technology.

Keywords: Postharvest Preservation, Nutritional Value, Packaging, Irradiation, Cold Plasma

the fresh keeping period of fruits and vegetables and maintain their high quality and safety is a hot topic for researchers engaged in postharvest preservation technology of fruits and vegetables.

Fruit and vegetable preservation technology can be divided into physical preservation, chemical preservation, and biological preservation. Traditional preservation techniques, such as heat treatment and chemical treatment, can provide effective preservation effects, but lead to the decline of fruit sensory quality and the loss of nutrients (Rawson et al., 2011). Moreover, heat treatment and chemical treatment cannot completely and effectively target all pathogenic microorganisms and the infection of microorganisms will bring danger and harm to human health and the social environment (Escalona et al., 2015). Hence, to meet the freshness, nutrition, and safety of fruits and vegetables, non-heat-treated fresh-keeping technology has been widely concerned and studied by scholars and enterprises. These non-thermal technologies, such as active packaging, irradiation, and cold plasma, are fantastic choices for the reason that they mitigate damage to the quality of fruits and vegetables (Hernández-Hernández et al., 2019). For instance, (Pace et al., 2020) demonstrated that active packaging containing oxalic acid significantly reduced



respiration rate, leaf edge browning, and electrolyte leakage, preserving the visual quality of fresh cut lettuce. This study reviews the current application research progress of several types of non-thermal preservation technologies based on the premise of ensuring the freshness, safety, and nutrition of fruits and vegetables. It aims to provide scientific researchers with guidance for the research and development of non-thermal preservation technology, which could be employed by the fruit and vegetable industry for fresh market use and juice processing and help production practitioners to improve the fresh keeping effect of fruits and vegetables by using non-thermal fresh-keeping technology.

Packaging Technology

The packaging of food is not only conducive to prolonging the fresh-keeping period but also beneficial to the protection of food from the external environment in the process of market circulation. At the same time, with the development of science and technology, especially nanotechnology and artificial intelligence, environment friendly food packaging materials, and intelligent packaging have attracted more and more attention from researchers (Hannon *et al.*, 2015).

Modified Atmosphere Packaging (MAP)

Fruits and vegetables are still complete organisms after harvest, undergoing respiratory metabolism and energy metabolism under normal environmental conditions. MAP inhibits the respiration rate of fruit by reducing the proportion of oxygen and increasing the proportion of carbon dioxide, thereby reducing the consumption rate of the substrate. Especially for climacteric fruits and vegetables, ethylene, as a plant hormone, plays a very important role in the ripening and aging process of fruits and vegetables. The hypoxic environment of MAP can significantly reduce the biosynthesis of ethylene, thereby delaying the ripening and senescence of fruits and vegetables and maintaining their higher nutritional value of fruits and vegetables (Sandhya, 2010).

Modified atmosphere packaging is widely used in the preservation of fresh fruits and vegetables or lightly processed fruits and vegetables to achieve the effect of extending shelf life and maintaining quality (Table 1). For different varieties, the changes in gas composition ratio will have different effects. As proof, Wang and Long (2014) showed that modified atmosphere packaging containing 1.8-8.0% O₂ reduced the respiration rate of cherries and the degradation of organic acids and effectively maintained the flavor of cherries; while Li *et al.* (2012) used MAP (O₂ 80%) significantly increased the polyphenol content of pear fruit; (Oms-Oliu *et al.*, 2008) used a high concentration of oxygen to inhibit the enzymatic reaction and maintain a higher fruit firmness of melon fruit. In addition, the effect of modified atmosphere packaging is

also significantly related to the packaging material and storage temperature. The air permeability of packaging materials is an important factor affecting the effect of modified atmosphere packaging and the reason why the effect of modified atmosphere packaging is regulated by temperature is that it directly affects the metabolic rate of harvested vegetables (Zhang *et al.*, 2016). Modified atmosphere packaging can not only affect the physiology of fruits and vegetables after harvest but also effectively prevent the infection and destruction of fruits and vegetables, such as mango (Poubol and Izumi, 2005), papaya (Waghmare and Annapure, 2013), strawberries (Van der Steen *et al.*, 2002), etc., (Table 1).

Active Packaging (AP)

Active packaging refers to a packaging technology that adds auxiliary materials to the packaging system to improve the storage environment, thereby maintaining the quality and safety of food and extending its shelf life of food (Mihindukulasuriya and Lim, 2014). With the continuous research and development of active packaging technology, increasing numbers of researchers have begun to explore the application of active packaging in the preservation of fruits and vegetables (Table 2). Packaging made of Polypropylene/Ethylene Vinyl Alcohol (PP/EVOH) film containing essential oils can significantly restrain the growth and reproduction of pathogenic microorganisms Escherichia coli, Salmonella, and Listeria monocytogenes, thereby that can improve the safety of salad and extend its shelf life (Muriel-Galet et al., 2012). The Ag⁺ based active membrane showed a significant inhibitory effect on the proliferation of acidophilic heat-resistant bacteria (Nobile et al., 2004). Li et al. (2011) developed a package prepared by coating PVC film with nano-ZnO powder, which can effectively suppress the browning rate of fresh-cut apples and maintain the quality better. It can be seen that active packaging can not only effectively maintain fruit quality, but also significantly inhibit microbial infection and delay fruit ripening and senescence.

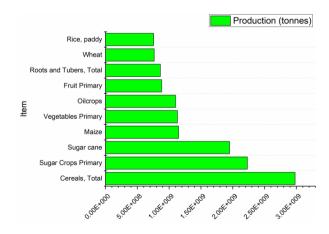


Fig. 1: Global production of major crops

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Object	Technology	Optimal condition	Effects	Remaining nutritional value	References
Apple	MAP	Calcium ascorbate + MAP	Delay fruit ripening and senescence	Higher Vc content and	
				antioxidant properties	Aguayo et al. (2010)
Mango	MAP	60 kPa O ₂ 5°C	Depressed breathing rate; inhibit browning	ns	Poubol and Izumi (2005)
Pear	MAP	80% O ₂	Increase polyphenol content	Higher polyphenol	Li et al. (2012)
Tomato	MAP	10% O ₂ +10% CO ₂	Delayed color volution; reduced the firmness loss and decay rate	Slightly lower TSS and TA at end of storage; higher lycopene and β -carotene	Olveira-Bouzas <i>et al.</i> , (2021)
Straw berry	/ MAP	5% O ₂ +15% CO ₂	Highest fruit firmness and the lowest weight loss;	TSS and TA are slightly higher then the control	Blaszczyk <i>et al.</i> (2022)
Pepper	MAP	MAP	Less fungal proliferation	ns	Frans et al. (2021)

Table 1: Application of MAP in the preservation of postharvest fruits and vegetables

Vc: Vitamin C/ascorbic acid; TSS: Total Soluble Solids; TA: Total Acid; kPa: Kilopascal; O2: Oxygen; CO2: Carbon dioxide; C2H4: Ethylene; ns: Not significant

Table 2: Application of AP in the preservation of postharvest fruits and vegetables

Object	Technology	Optimal condition	Effects	Remaining nutritional value	References
Straw berry	AP	Oxygen absorber	Hold fruit firmness; reduce rot rate	Higher TSS	Aday and Caner (2013)
Straw berry	AP	Oregano essential oil	Reduce respiration rate; maintain firmness	Higher TSS and TA	Li et al. (2020)
Grape	AP	EOs-β-cd inclusion Complex	Reduce weight loss, Microbial growth	Higher TA and TSS	Lopez-Gomez <i>et al.</i> (2020)
Nectarine	AP	EOs-β-cd inclusion complex	Higher hardness; better sensory quality	Higher TA and TSS	Lopez-Gomez <i>et al.</i> (2020)
Lettuce	AP	EOs-β-cd inclusion complex	Less weight loss; better sensory quality	Higher TA and TSS	Lopez-Gomez <i>et al.</i> (2020)

Absorber: Strong adsorption capacity for adsorbate

EOs-β-cd inclusion complex: β-cyclodextrin-essential oils inclusion complex

Although there has been a lot of research in the field of active packaging, only a few antibacterial and antioxidant packaging technologies have been put on the market and most of the research focuses on the screening of antibacterial and antioxidants.

Intelligent Packaging (IP)

Intelligent packaging is a packaging system with smart functions. It can assist in precise artificial control through functions such as detection, recording, tracking, feedback, and warning, to prolong the storage period of fruits and vegetables and maintain higher quality (Ahvenainen and Hurme, 1997). With the development of science and technology, new packaging systems have been rapidly developed and extensively studied. Mills and Hazafy (2008) developed a UV-B-activated oxygen indicator using nanoparticulate tin oxide as a Semiconductor Photosensitizer (SCP). In addition to chemical substances as receptors, some biosensors use biological materials as receptors, such as enzymes, antibodies, antigens, bacteriophages, and nucleic acids. Based on the principle of biosensors, SIRA technologies (USA) has developed a packaging barcode technology that alerts consumers or retailers if a product has been exposed to adverse conditions and poses a safety hazard (Ghaani et al., 2016). Based on the hydrolysis of esters, a ripeness indicator for aroma esters was developed for the first time by Hort Research (New Zealand) specifically for pears (Janjarasskul and Suppakul, 2018). At present, there are still huge challenges in the field of intelligent packaging. For example, there is a lack of indicators with high sensitivity and specificity and how to ensure their accuracy and stability.

Irradiation Technology

Irradiation technology, as a new type of physical nonthermal processing technology, mainly utilizes the radiation chemical and radiation microbiological effects produced by the radiation source, so as to achieve the purpose of sterilization, inhibition of germination, and delay of ripening and senescence of fruits and vegetables (Lung et al., 2015). Previous studies by some international authoritative institutions believed that irradiation technology can be used as a safe and efficient treatment method to replace the fumigation of chemical reagents for the preservation of fruits and vegetables (Pinela and Ferreira, 2017). With the rapid advancement of technology, the International Codex Alimentarius Commission (CAC) issued the "International General Standard for Irradiated Foods" and lifted the limit of the maximum absorbed dose of 10 kilograys (kGy) in food irradiation processing. Not only that, irradiation has the advantages of strong penetrating ability, easy control of the reaction, and simple processing flow, so it has great research value and application prospects. Tables 3-6 presents several examples of the application of irradiation techniques such as y-ray irradiation, Electron Beam Irradiation (EBI), ultraviolet, Pulsed Light (PL), and cold plasma in the preservation of harvested vegetables.

Gamma Ray Irradiation

Ionizing radiation is to use of radiation sources of 60 cobalt (60 Co) or 137 cesium (137 Cs) to treat food or packaging materials to achieve the purpose of maintaining quality and prolonging the storage period. Among them, 60 Co- γ ray has the advantages of strong penetrating ability, uniform irradiation intensity, and operational

reliability. Moreover, it is currently the most widely used irradiation processing technology at home and abroad.

Gamma-ray irradiation can effectively kill pathogenic microorganisms and prevent the infection of fruits and vegetables by microorganisms. The results of (Hussain et al., 2019) indicated that 0.9 kGy irradiation treatment can significantly inhibit the growth and reproduction of yeast and mold. Not only that, γ -ray irradiation can effectively delay the ripening and senescence of fruits and vegetables and significantly maintain their nutritional quality of fruits and vegetables (Table 3). Studies have shown that within a certain dose range, the respiration rate of postharvest fruits decreases with the increase of irradiation dose, which may be caused by the fact that irradiation reduces the activity of enzymes related to respiration and metabolism (Boynton et al., 2006). The results of (Maraei and Elsawy, 2017) illustrated that compared with the control, appropriate γ -ray irradiation effectively reduced the weight loss rate of strawberry fruit, maintained higher total phenolic content and antioxidant capacity, and thus maintained better nutritional quality. Through comparison, it is found that the optimal dose of γ -ray irradiation applied to fruits and vegetables of different species is different. The reason for this phenomenon mainly depends on the optimal dose that can be absorbed by fruits and vegetables and the absorbed dose is related to its quality, density and thickness, and other factors.

Electron Beam Irradiation (EBI)

Different from ionizing gamma rays with a radiation source, electron beam irradiation is to generate electron beams with a certain energy through an electron accelerator and then irradiates the object. Compared with γ -ray irradiation, electron beam irradiation has the following advantages: (1) No radioactive waste is generated and there is no hidden danger of environmental pollution; (2) The processing speed is fast and the product performance is less degraded; low cost to build and operate.

With the continuous development and improvement of electron beam irradiation technology, it has been widely used in many fields. It can be seen from Table 4 that electron beam irradiation can reduce microorganisms, reduce the loss of nutrients and maintain higher storage quality in fruits and vegetables. Schmidt et al. (2006) found that low-dose electron beam irradiation could significantly inhibit the reproduction of Salmonella in tomato fruit. The results of (Truc et al., 2021) showed that electron beam irradiation could defer the decline of firmness of postharvest mango, delay the increase of Total Soluble Solids (TSS) and stay the ripening and senescence of mango. Although there are many studies on the effect of EBI on the preservation of fruits and vegetables after harvest, a lot of research is needed on the response effect of specific quality parameters of fresh fruits and vegetables on the dose of EBI. At the same time, it is necessary to increase publicity and promotion work to promote the commercial application of this technology.

Ultraviolet (UV) and Pulsed Light (PL)

Ultraviolet rays are electromagnetic waves with frequencies between visible light and X-rays, with wavelengths ranging from 10 to 400 nm. According to the wavelength range, ultraviolet rays can be divided into low frequency long-wave ultraviolet (UV-A, wavelength 320 ~ 400 nm), intermediate frequency medium-wave ultraviolet (UV-B, wavelength 280 ~ 320 nm), high-frequency short wave ultraviolet (UV-C, Wavelength 100 ~ 280 nm) and ultra-high frequency ultraviolet (EUV, 10 ~ 100 nm). Among them, the main wavelength band that causes biological effects is short wave ultraviolet rays ranging from 100 to 280 nm. Syamaladevi et al. (2015) showed that UV-C irradiation treatment can effectively reduce the expansion of Penicillium on the surface of the apple, cherry, and strawberry fruits. In addition, UV-C treatment can effectively inhibit the production of tomato ethylene, delay the decline of firmness and then retard fruit ripening and senescence (Severo et al., 2015). It can be seen that UV-C irradiation can not only promote the resistance of fruits and vegetables to postharvest diseases but also effectively delay the ripening and senescence of fruits and vegetables.

Pulse strong light is the use of an inert gas discharge light source in the frequency range of 200 ~ 1100 nm to generate high power, short term strong broad-spectrum pulsed light radiation, also known as high-intensity pulsed ultraviolet light, strong light pulse, broad-spectrum white light, etc. In the field of food sterilization, a large number of studies have proved that pulsed light can effectively inactivate microorganisms. The research of (Aguiló-Aguayo et al., 2013) indicated that PL treatment effectively inhibited the nutrient loss of tomato fruit. Ramesh et al. (2012) found that PL treatment significantly increases the total phenolic content and antioxidant capacity of elderberry. Charles et al. (2013) showed that PL treatment resulted in higher firmness and flavonoid content in fresh cut mangoes, effectively delaying fruit softening and nutrient loss. At present, most of the research focuses on the study of PL treatment on the safety and nutritional quality of fruits and vegetables. However, the molecular regulation mechanism of PL in regulating the quality of fruits and vegetables needs to be further explored.

Cold Plasma (CP)

Plasma is the fourth state of matter after solid, liquid, and gas. When the applied voltage reaches the breakdown voltage, the gas molecules are ionized, resulting in a mixture of electrons, ions, atoms, and atomic groups. In the process of low-temperature plasma discharge, although the temperature of electrons is high, the temperature of heavy particles is very low and the whole system is in a low-temperature state, so it is called cold plasma, also called non-equilibrium plasma.

The generation of cold plasma mainly includes glow discharge, corona discharge, dielectric barrier discharge, radio frequency discharge, and other methods. The research of cold plasma technology has been greatly developed in the fields of semiconductors, the coal chemical industry, the synthesis of new substances and new materials, and the food industry. Cold plasma is rich in a mass of active substances, such as ions, electrons, molecules, and free radicals, which have the ability to kill microorganisms. The experimental result of (Yong *et al.*, 2015) proved that CP treatment

could effectively deal with Salmonella typhimurium, Escherichia coli, and Listeria on the surface of the cheese. The experimental result of (Tappi *et al.*, 2019) found that CP treatment could effectively alleviate the browning of fresh cut apples. Wang and Long (2014) detected that CP can reduce the rot rate of blueberries and induce the activity of antioxidant enzymes in blueberries through its bactericidal effect, thereby improving the quality of blueberries during storage. Therefore, CP can not only effectively destroy pathogenic microorganisms on the surface of fruits and vegetables, but also significantly preserve the storage quality of fruits and vegetables (Table 7).

Table 3: Application of gamma irradiation in the preservation of postharvest fruits and vegetables

Object	Technology	Optimal condition	Effects	Remaining nutritional value	References
Grape	γ-ray	0.5-1.0 kGy (Helwani)	50% longer shelf-life	nm	Al-Bachir (1999)
		1.5-2.0 kGy (Baladi)			
Papaya	γ-ray	1.8-2.1 kGy	Curb corruption; extend shelf-life	Higher chlorophyll	Hussain et al. (2019)
Tomato	γ-ray	1-4 kGy	Lower weight loss	Higher TSS	Gyimah et al. (2020)
Jujube	γ-ray	1.0 kGy	Enhance antioxidant potential	Higher ascorbic acid and total phenol content	Jat <i>et al.</i> (2022)
Fresh-cut peach	γ-ray	up to 1.0 kGy	Extend shelf-life	ns	Colletti et al. (2022)
Pomegranate	γ-ray	1.0 kGy	Reduce the population of bacteria,		
			fungi and yeasts; increase the shelf-life	ns	Ashtari et al. (2019)

kGy: Kilogray; nm: No mention

Table 4: Application of EBI in the preservation of postharvest fruits and vegetables

Object	Technology	Optimal condition	Effects	Remaining nutritional value	References
Mango	EBI	0.5 kGy	Inhibit chlorophyll degrading enzyme activity; enhance antioxidant capacity	Higher chlorophyll	Nguyen et al. (2021)
Mango	EBI	0.5 kGy	Alleviate disease; maintain quality	Higher TA; lower TSS	Truc et al. (2021)
Mango	EBI	0.5 kGy +13°C	higher firmness	Higher contents of cell wall polysaccharides; lower content of water-soluble pectin	Nguyen et al. (2021)
Kiwifruit	EBI	0.5 kGy +1°C	Keep higher quality	Higher TA, TSS, and Vc content	Zhou et al. (2015)
Kiwifruit	EBI	0.5 kGy +0-1°C	Higher firmness; improve activity	Reduce the content of malondialdehyde	
		·	of antioxidant enzymes;	lower TSS content	Li et al. (2021)
Straw berry	EBI	1.0 kGy +4°C	Reduce the population of fungi and the bacterial mesophilic; extend the shelf-life of up to 7 days	Lower total phenolic and total flavonoid contents	Barkaoui <i>et al.</i> (2021)

Table 5: Applic	Table 5: Application of UV in the preservation of postharvest fruits and vegetables						
Object	Technology	Optimal condition	Effects	Remaining nutritional value	References		
Grape	UV-B	5.98, 9.66 kJ m ⁻² d ⁻¹	Induction of phenol production		Martínez-Lüscher et al. (2014)		
Straw berry	UV-C	4.1 kJ m ⁻²	Maintains hardness, inhibits mature aging	Less TSS and anthocyanins	Li <i>et al</i> . (2014)		
Broccoli florets	UV-B	1.5 kJ m ⁻²	Delay the yellowing; increase antioxidant capacity	Higher indole-type glucosinolates and hydroxycinnamates contents	Duarte-Sierra et al. (2020)		
Tomato	UV-A	6.0 kJ m ⁻²	Enhance antioxidant activity	Higher contents of total phenol	Dyshlyuk et al. (2020)		
Sweet cherry	Chitosan + UV-B + UV-C	21.6 kJ m ⁻²	Reduce weight loss; highest fruit firmness	Higher vitamin C and total phenolic compounds	Abdipour et al. (2020)		

Table 6: Application of PL in the preservation of postharvest fruits and vegetables

Object	Technology	Optimal condition	Effects	Remaining nutritional value	References
Fig	PL	90~300 s	Stimulates the accumulation of anthocyanins	of More anthocyanins	Rodov et al. (2012)
Tomato	PL	1~8 J cm ⁻²	Enhances antioxidant capacity	Higher contents of antioxidants	Pataro et al. (2015)
Persimmon	PL	2 J cm ⁻² or 6 J cm ⁻²	Provoke antioxidant capacity	No impact on TSS and vitamin C;	Denoya et al. (2020)
				higher contents of total phenols	
Straw berry	PL	3 J cm ⁻²	Slightly reduce the level of Salmonella	Not significant	Cao et al. (2019)
Apricot	PL	200 J 60 s	Inhibit microbial growth; increase	Higher total phenols,	Hua et al. (2022)
			antioxidant capacity; reduce cell	total flavonoids	
			structure damage		

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Object	Technology	Optimal condition	Effects	Remaining nutritional value	References
Blueberry	СР	Spray volume 4 cfm, ambient air volume 7 cfm, working distance 7.5 cm, duration 60 s	Reduce rot rate and maintain a higher edible quality	ns	Lacombe <i>et al.</i> (2015)
Fresh-cut apple	СР	Plasma-activated water treatment with a sinusoidal voltage of 7.0 kHz and an the amplitude of 8 kV for 5 min	Inhibit the growth and reproduction of microorganism	ns	Liu <i>et al.</i> (2020)
Fresh-cut mango	СР	75 kV for 3 min using a Dielectric Barrier Discharge (DBD) generator	Inhibits the ROS generation and membrane lipid peroxidation and the growth of total microbial counts	Higher TSS, TA carotenoids	Yi et al. (2022)
Soybean sprouts	СР	cold-plasma- activated water	Sprout length and fresh weight increased by 41.07,11.24% respectively	Higher total amino acid and contents of isoflavone	Ji <i>et al</i> . (2022)

Table 7: Application of cold plasma in the preservation of postharvest fruits and vegetables

Summary and Outlook

With rapid economic and social development, people's demand for fresh fruits and vegetables is increasing. However, issues such as food safety and postharvest quality have seriously affected the circulation and economic value of harvested fruits and vegetables. On the premise of ensuring food safety, the non-thermophysical fresh keeping technology not only holds the better sensory quality and nutritional value of the harvested vegetables but also effectively postpones their maturity and aging. Based on the characteristics of safety, efficient and green non-thermal physical preservation technology has received extensive attention. However, the vast majority of studies mainly discuss its effects on the physiological quality and freshkeeping effect of post-harvest fruits and vegetables. In the future, the following aspects should be strengthened: (1) To explore the combined application of various nonthermophysical fresh-keeping technologies on the quality and preservation of post-harvest fruits. (2) From the perspective of transcriptional regulation, the molecular mechanism of preservation technology to maintain postharvest fruit quality and delay ripening and senescence was explored; (3) Based on the latest scientific research results, develop non-thermal Physical preservation equipment, accelerate the transformation of scientific and technological achievements and significantly improve the market circulation and economic value of fresh fruits and vegetables.

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Author's Contributions

Shuai Han: Initiated the concept of the article and wrote.

Hongfang Cai: Initiated the concept of the article and contributed to the summary and outlook.

Youzhi Wu and Haitao Yu: Contributed to the proofread of the manuscript.

Haihua Cong: Provided modification suggestions and polished the manuscript.

Ethics

This article is original and contains unpublished material. The corresponding author confirms that all of the other authors have read and approved the manuscript and no ethical issues are involved.

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