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High-Pressure Carbon Dioxide Used for Pasteurization in Food Industry

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Abstract

The demand for safe, high-quality food has greatly increased, in recent times. As traditional thermal pasteurization can significantly impact the nutritional value and the color of fresh food, an increasing number of nonthermal pasteurization technologies have attracted attention. The bactericidal effect of high-pressure carbon dioxide has been known for many years, and its effect on food-related enzymes has been studied. This novel technology has many merits, owing to its use of relatively low pressures and temperatures, which make it a potentially valuable future method for nonthermal pasteurization. For example, the inactivation of polyphenol oxidase can be achieved with relatively low temperature and pressure, and this can contribute to food quality and better preserve nutrients, such as vitamin C. However, this novel technology has yet to be developed on an industrial scale due to insufficient test data. In order to support the further development of this application, on an industrial scale, we have reviewed the existing information on high-pressure carbon dioxide pasteurization technology. We include its bactericidal effects and its influence on food quality. We also pave the way for future studies, by highlighting key areas.

Keywords Nonthermal pasteurization · High-pressure carbon dioxide · Food industry · Bactericidal effect · Food quality

Introduction

The consumer demand for better food safety, quality, and nutritive value has been increasing. However, traditional thermal pasteurization technologies can destroy the content of food. Furthermore, the color of food is always altered by traditional thermal pasteurization methods which may reduce the value of food products [1].

Hence, in recent years, an increasing number of nonthermal pasteurization technologies have been studied by leading scientists in the fields; these technologies entail the use of high hydrostatic pressure, ultraviolet (UV) irradiation, ultrasound, high-pressure carbon dioxide (HPCD), high-pressure homogenization, and microfiltration.

Since Valley and Rettger, in 1927, discovered the bactericidal effect of pressurized CO_2, an increasing number of scientists have conducted research on HPCD inactivation in microorganisms, as a novel nonthermal pasteurization technology for the food industry. In the year 2012, the number of published papers about HPCD inactivation on food increased notably (Fig. 1). Although HPCD pasteurization has yet to reach a large commercial scale, more people are realizing its potential as a technology for food pasteurization, following significant, positive results from research concerning its bactericidal effect [2]. HPCD is a novel nonthermal pasteurization technology that applies pressurized CO_2 at ≥ 0.1 MPa (1 bar), at a relatively low temperature (lower than thermal pasteurization). Carbon dioxide presents different phases at different temperatures and pressures (Fig. 2). Above critical conditions (7.38 MPa, 31.1 °C or 73.8 bar, 304.25 K), CO_2 always exists as a supercritical fluid, which has properties of gas and liquid [3]. Until now, HPCD inactivation studies have generally been conducted at temperatures ranging from room temperature (25 °C or 298.15 K) to 100 °C (373.15 K) and pressures ranging from 0.1 to 50 MPa. Hence, for HPCD inactivation technology, carbon dioxide is generally found in the gas phase or as a supercritical fluid (Fig. 2).

In this review, we present a simple introduction to current pasteurization technologies, followed by a

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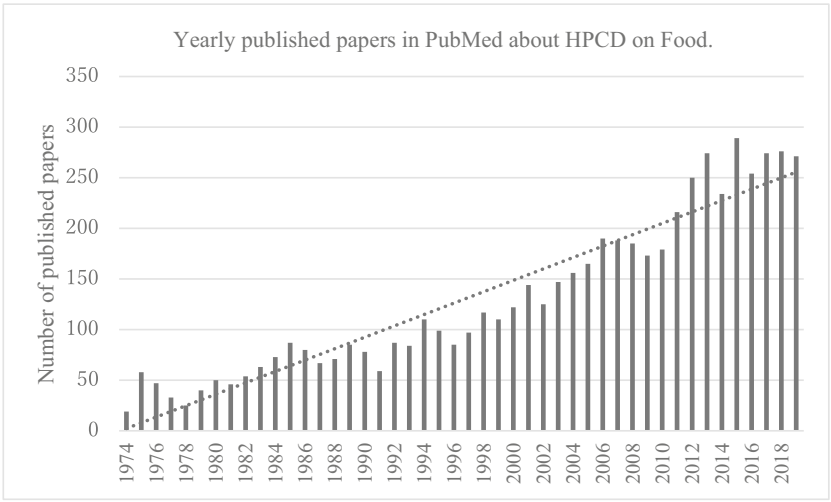

Fig. 1 The yearly published papers in PubMed about high-pressure carbon dioxide on food

discussion of the applications of HPCD in the food industry, including the inactivation of bacteria, spores, and viruses. The lack of clarity and details regarding the mechanisms of HPCD inactivation of microorganisms is a major obstacle to its industrial application. Therefore, possible mechanisms of bactericidal activity are fully discussed in this review, including information from recent studies. The effects of HPCD on food quality and nutritive value are also introduced. Many studies have showed that HPCD could be a useful alternative pasteurization technique providing better nutrition and contributing to food quality by inactivating some enzymes. In this paper, we also discuss the issues of HPCD technology, faced by the food industry, and present some suggestions for future work. Our aim is to stimulate future interest in the application of HPCD nonthermal pasteurization technology in the food industry.

The Introduction of Pasteurization Technologies in the Food Industry

High Hydrostatic Pressure

High hydrostatic pressure (HHP) is currently the most used and developed industrial, nonthermal decontamination technology. Since HHP and HPCD both apply pressure, a great description of HHP is given here, compared with other technologies, such as thermal pasteurization, irradiation, ultrasound, and pulsed electric fields. Japan was the first country, in 1990, to start commercial food processing of fruit jams with HHP. After that, an increasing number of commercial applications of HHP were developed by the food industry [4]. Generally, pressures of 100~600 MPa are applied for commercial pasteurization by HHP. However, pressures in this range cannot satisfy the requirements of commercial steriliza-

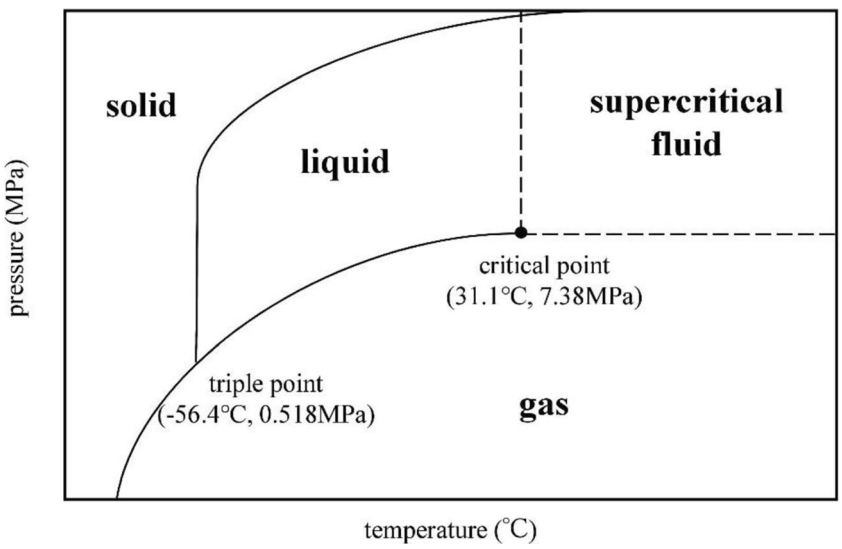

Fig. 2 Schematic representation of carbon dioxide phase diagram

tion, since they are unable to destroy bacterial spores. The temperature should be moderately raised (90~120 °C) in combination with HHP, to achieve commercial sterilization [5, 6].

The mechanisms and factors of HHP pasteurization on microorganisms have been well discussed in some reports. The alteration of membranes is considered to be the main lethal mechanism [6, 7], and damage to the nuclear membrane has been described as the lethal factor in yeast cells [8, 9].

The irreversible denaturation of proteins was also observed after HHP treatment. This would include the inactivation of enzymes that normally limit the storage period [6]. The same result was confirmed by Buzrul [10]. It has also been reported that this technology can maintain the stability of fatty acids, which play a significant role in the sensory characteristics of meat [11]. It should be noted that a higher fat content will decrease the efficiency of HHP in the inactivation of bacteria [12].

Packaged food is frequently submerged in water, in a tank, prior to HHP treatment. Generally, the temperature of is maintained at ≤ 30 °C even when the pressure increase to 600 MPa, which can preserve the food taste, color, flavor, nutrition, and extrinsic features as far as possible, compared with traditional thermal pasteurization [6, 13, 14]. Water is usually used as a pressure transmission medium. Hence, pressure can be transmitted to all points, to ensure uniform pasteurization without consideration of composition, shape, or size. However, when food is treated inside its packaging, it should have the ability to survive volume reductions of up to 15% [15].

Due to the high cost of investment, the price of HHP processed food is high. Therefore, the application of HHP is only an appealing choice for the market in higher-priced, healthier food products. HHP processed food is considered to contain more nutrition and provide more health benefits than food pasteurized by traditional methods [4, 16]. This is also a good choice for extracting medicinal products with higher bioactivity and higher efficiency [17].

Thermal Pasteurization

The two best known thermal pasteurization methods are "low-temperature long time" and "high-temperature short time," which are widely applied to milk pasteurization. To maintain the chemical, physical, and sensory qualities of pasteurized milk, ultra-high-temperature processing (UHT) was developed. UHT processing generally uses a high temperature for a short time, such as 150 °C for 2 s. However, thermal pasteurization methods have many disadvantages for food ingredients and always influence the color of the product, which may then influence the product value [1, 18].

Irradiation

In this section, two main irradiation technologies for pasteurization are introduced: pulsed light technology and microwave radiation, which are both examples of non-ionizing radiation.

Pulsed light technology uses inert gas flash lamps to generate short-duration, high-power pulses across a broad spectrum. The wavelength range is from 200 to 1000 nm [19]. It has been shown that pulsed light technology can effectively inactivate various microorganisms [20–22]. Pulsed UV light is the most commonly used method that can destroy the conjugated carbon = carbon double bonds in proteins and nucleic acids, followed by structural changes in the DNA, leading to cell death [20]. This technology has an approved ability to enhance food nutrition, without other properties being changed, compared with traditional thermal pasteurization [23], including the reduction of allergens which can provide consumers with healthier food [24, 25]. However, pulsed light technology is generally considered as more suitable for surface pasteurization, for example, for decontamination of packaging. This is because light can be both absorbed and scattered by food, leading to lower decreased decontamination efficiency inside the food [26].

Microwave radiation is another radiation, with wavelengths from 1 to 1000 mm and frequencies from 300 to 300,000 MHz. The translational motion of molecules, vibration of the lattice consisting of atoms or ions, and the elevation of free electron energy in metals can all be induced by the electric and magnetic field interactions of microwaves. Microwave energy is absorbed by materials and converted to heat, which leads to microbial and enzyme inactivation [27, 28]. Microwave radiation has been widely used in the industrial food pasteurization process, to provide higher quality products by inactivating key pathogens, enzymes, and bacteria. Microwave power, resultant temperature, and treatment time can all influence the inactivation efficiency for bacteria [29]. However, because the heating process is volume-dependent, it is difficult to pasteurize materials in bulk, using microwaves.

Pulsed Electric Fields

Pulsed, high-voltage electric fields are mainly applied to the pasteurization of liquid food. Consequently, electropermeabilization of microorganisms can be induced, due to the influence of the electric field on the charged molecules in their membranes. The formation of pores in membranes is followed by cell death [30]. In addition, pulsed electric fields can inactive some enzymes by disordering their secondary or tertiary structures, leading to a conformational change [31]. Pulsed electric fields can effectively inactivate microorganisms, and some enzymes, providing safe and stable food, and can also maintain or enhance the nutritional value. For

example, in wines treated with pulsed electric fields during the storage stage, a higher retention of phenolics and less degradation of volatiles has been observed [32]. The antioxidant activity of pine nut peptides can be improved by pulsed electric field treatment [33]. A higher concentration of carotenoids in fruit juice-skim milk and fruit juice-whole milk beverages was also observed [34]. The influence of pulsed electric fields on food nutrition and physicochemical properties has been well discussed by Gabric et al. [35].

Ultrasound

Ultrasound is a nonthermal pasteurization method that applies ultrasonic waves to rapidly initiate the formation of a large number of small bubbles, in liquids, which subsequently collapse, triggering disruption of cell membranes and damage to DNA [36]. The bactericidal effects of ultrasound have been identified in many microorganisms, such as *Saccharomyces cerevisiae* and *Escherichia coli* [37, 38]. Ultrasound pasteurization technology has great advantages for food processing because of its ability to preserve food quality, compared with traditional thermal pasteurization [39]. However, it requires a relatively long exposure, which can also impair food quality [40].

High-Pressure Carbon Dioxide

High-pressure carbon dioxide (HPCD) is a type of nonthermal pasteurization that applies pressurized CO_2, at between 0.1 MPa (1 bar) and 50 MPa (500 bar). Compared with HHP pasteurization technology, HPCD uses less sophisticated equipment, since most microbes can be inactivated at under 50 MPa. HPCD possesses great potential as a novel, nonthermal pasteurization technology, and the bactericidal effects on various microorganisms and the influence of HPCD on nutritional compounds are the main subjects of this review.

Apart from the aforementioned pasteurization technologies, there are other nonthermal methods that have been studied by scientists. High-pressure homogenization, ultrafiltration, and microfiltration are the most commonly used membrane filtration techniques for fruit juice processing, and there are chemical methods, such as the use of natural antimicrobials [41–43].

Factors Influencing the Inactivation Effect of HPCD

The bactericidal effect of compressed CO_2 has been known for nearly a hundred years [44]. It has been shown that the efficiency of HPCD in microorganism inactivation is related to many factors. Since many of these factors influence pasteurization efficiency, to varying degrees, a discussion of HPCD inactivation factors should be presented here. We also expect this to provide useful guidance for industrial operation.

Microorganism Species

The bactericidal effects of HPCD on various bacteria have been well studied by scientists (Table 1). Different bacteria present different responses to HPCD treatment. It was observed that aerobic psychrophilic microorganisms are much more sensitive to HPCD than aerobic mesophilic microorganisms [50]. Furthermore, *L. monocytogenes* is much more sensitive than *E. coli* to HPCD treatment [52].

However, no pattern of bactericidal effect was found between gram-positive bacteria, gram-negative bacteria, or fungi, as far as current research goes. This suggests that the bactericidal effects of HPCD have no significant connection with the cell wall. Nevertheless, in the interest of scientific understanding, more research needs to be conducted to clarify the bactericidal effects of HPCD on gram-positive and gram-negative bacteria, and on fungi, by varying and controlling the treatment conditions (temperature, pressure, time, and medium).

Although bacterial vegetative cells can be easily inactivated by HPCD, their spore forms are more difficult to inactivate by HPCD, in the same conditions of pressure, time, and temperature. For example, a relatively high temperature (~ 85 °C) combined with 20 MPa HPCD for 60 min is needed, to effectively inactivate spores of *Bacillus subtilis* [53]. However, more than 7 log reduction of vegetative cells of the same species can be completed by treatment at 38 °C and 7.4 MPa for just 2.5 min [54]. The resistance of spores to HPCD has been ranked as follows: *B. subtilis* > *G. stearothermophilus* > *B. licheniformis* > *B. coagulans* > *B. cereus* [55].

It was also discovered that HPCD can inactivate bacteriophage T4 [2]. About a 4.0 log reduction for bacteriophage T4, > 3.0 log reduction for bacteriophage MS2, > 3.3 log reduction in bacteriophage Qβ, and just under a 3.0 log reduction in bacteriophage ΦX174 were all achieved at 0.7 MPa for 25 min at 22 °C [56, 57].

Cell Concentration

Bacterial samples with a higher concentration of cells show a lower efficiency of inactivation by compressed carbon dioxide than low-concentration samples [52]. When higher concentrations were treated with pressurized CO_2, more cells clumped, which made it difficult for CO_2 to penetrate the cell membranes, leading to a decreased bactericidal effect. Consequently, in real industrial applications, the initial concentration of cells should be taken into consideration for the pasteurization of biomass by HPCD.

Table 1 Inactivation of HPCD on microorganism. *AMM* (aerobic mesophilic microorganisms); *APM* (aerobic psychrophilic microorganisms); *SPS* (sterile physiological saline); *CSF* (coho salmon fillets); *RCBM* (raw chicken breast meat); *RT* (room temperature); *HHP* (high hydrostatic pressure)

Microorganism species	Solution	HPCD condition	Additional technique	Inactivation efficiency	Reference
Escherichia coli	Pineapple juice	10 MPa, 31 °C, 3.06 min	Ultrasound	Total inactivation	[45]
Wet *E. coli AW1.7*	LB broth	35 °C, 15 min, 10 MPa	No	More than 3 log (CFU/ml) reduction	[46]
Dry *E. coli AW1.7*	Dry	35 °C, 15 min, 10 MPa	No	Less than 0.5 log (CFU/ml) reduction	[46]
Yeast	Pineapple juice	10 MPa, 31 °C, 3.06 min	Ultrasound	Total inactivation	[45]
Yeasts and molds	Strawberry juice	60 MPa, 40 °C, 30 min	No	Total inactivation	[47]
Vibrio parahaemolyticus	SPS	25 MPa, 40 °C, 10 min	No	5.69 [− Log(N/N0)]	[48]
Vibrio parahaemolyticus	SPS	25 MPa 40 °C, 40 min	No	7.02 [− Log(N/N0)]	[48]
Saccharomyces pastorianus	SPS	43 °C, 1 MPa, 1 min; 37 °C, 2 MPa, 1 min	5% ethanol addition	6 log reduction (both)	[49]
AMM	CSF	RT, 5 min, 150 MPa + 70% CO_2	HHP	0.43 log reduction	[50]
APM	CSF	RT, 5 min, 150 MPa + 70% CO_2	HHP	More than 0.67 log reduction	[50]
Mesophilic viable bacteria	Pineapple juice	10 MPa, 31 °C, 3.06 min	Ultrasound	Total inactivation	[45]
Mesophiles	RCBM	14 MPa, 40 °C, 45 min	No	2.99 Log CFU/g reductions	[51]
Yeasts and molds	RCBM	14 MPa, 40 °C, 45 min	No	4.01 Log CFU/g reductions	[51]

pH and Water Content

Some authors found that the efficiency of microbial inactivation by HPCD could be enhanced by decreasing the initial environmental pH [58]. However, regardless of the treatment pressure, the strain of microorganism, or exposure time, the pH of the endpoint after carbon dioxide treatment showed no significant difference [52]. The effect of pH was also investigated when the bacteriophage virus MS2 was treated with HCl (hydrochloric acid) under the same pressure as used for HPCD, and CO_2 treatment presented a higher sterilization effect than HCl treatment [57]. Hence, the pH decrease, which is induced by HPCD, is not the reason for microbial inactivation, but a lower initial environment pH can still improve the efficiency of inactivation.

Water has an important role in the inactivation efficiency of HPCD. A higher water content could enhance bactericidal efficiency. It has been suggested that wet cells are more sensitive to HPCD than dry cells [46]. For example, when wet *E. coli* in lysogeny broth was treated at 35 °C at 10 MPa with HPCD, for 15 min, cell colonies were reduced by more than 3 log (CFU/mL). However, when the dry *E. coli* was placed in the same conditions, cell colonies were reduced by < 0.5 log (CFU/mL). Other researchers have also demonstrated that water content plays an essential role in the bactericidal effect of HPCD [59]. Generally, HPCD technology presents a better inactivation efficiency for liquid materials compared to solids.

Physical State of Carbon Dioxide

One interesting study showed that gaseous CO_2 presents higher inactivation efficiency than supercritical CO_2 or liquid CO_2. In particular, when dry *E. coli* was treated with HPCD, more bactericidal activity can be accomplished with gaseous CO_2, whereas dry *E. coli* are resistant to treatment by supercritical and liquid CO_2 at the range of temperatures used [46]. However, a slightly higher temperature (~ 65 °C) is still required for effective inactivation of dry *E. coli*.

Treatment Time, Pressure, and Temperature

Generally, CO_2 treatment had an enhanced efficiency in cell destruction when the duration of exposure was increased. For example, 1.4 log CFU/g reduction of *E. coli* can be achieved after 15 min of treatment, whereas a 45-min treatment can induce up to 5 log reduction [51]. However, longer treatment periods are not always worth the effort to increase inactivation. Fleury et al. [52] found that the efficiency increased with time, until the treatment period reached a certain point, and there was no further improvement at 50 °C, even when the treatment was prolonged.

A higher inactivating effect of CO_2 could be achieved by using higher pressure [46, 47]. Higher pressure can enhance

CO_2 solubilization, facilitating its contact with and penetration into cells, which could explain the higher inactivation efficiency. Higher pressure can generate the same inactivation efficiency, at lower temperatures, as lower pressure can at a higher temperature [49]. Pressure has a positive effect on HPCD inactivation efficiency, but is not as important as temperature [52].

Among all the factors, temperature is considered to be the most important, to inactivate bacteria. However, temperature is not a factor to be regarded independently for bacterial inactivation. Similar pictures of cell cytoplasmic damage were observed at 38 °C and 50 °C, but only the higher temperature could achieve complete inactivation [52]. Despite this evidence, other studies suspect that pressure is the main lethal factor. According to them, a higher pressure can induce a decrease in pH, which leads to microbial inactivation [47].

Garcia-Gonzalez et al. [60] described the schematic survival curves of bacteria with HPCD treatment. They explained that, during the HPCD process, the shapes of survival curves are related to the number of experimental data, the treatment time, and the pressure applied. Generally, sufficient experimental data tend to present a concave curve. However, fewer data are prone to show a log-linear curve (Fig. 3a, b), but when the pressure is increased, the shape of the curve is converted to concave (Fig. 3a).

Combination with Other Technologies and Additives Effects

Other factors also have some influence on the bactericidal effect of HPCD, such as agitation, the physicochemical environment, and some additives. Appropriate agitation can enhance the bactericidal efficiency of HPCD [61]. The microbial inactivation rate could be enhanced by certain additives, such as ethanol [49]. Especially for spores, additives can greatly increase the inactivation effect at relatively mild temperatures (35–60 °C) [62–64]. When ultrasound is combined with HPCD, total inactivation can be reached in just 3 min, under 10 MPa, at 31 °C [45]. Another study, using HHP with HPCD, showed that the bactericidal effect is mainly due to the CO_2 content, and not the pressure, since a pressure of 150 MPa alone had no bactericidal effect, whereas CO_2 alone could inactive the bacteria without increased pressure [50]. It has also been suggested that using a pressure < 200 MPa for HHP is not effective in extending the storage period for salmon [65]. This suggests that pressure alone (at < 200 MPa) has a low efficiency of inactivation, without CO_2.

Inactivation Mechanism of HPCD

Mechanism of HPCD Inactivation in Vegetative Cells

Many scientists have tried to explain the inactivation mechanism of HPCD. Although the details are still unknown, some theories have been more widely accepted, and will be discussed here with reference to published work, including some new findings. Additionally, we provide a novel direction for future studies, to clarify and improve the mechanisms of HPCD inactivation. A schematic diagram of mechanisms for the inactivation of vegetative microbial cells is shown in Fig. 4.

A detailed interpretation is given, in points ⑤ and ⑥, since CO_2-induced membrane alternation is considered as the main reason for microbial inactivation.

①When bacterial cells are subjected to pressure, cell hydrophobicity will increase which can make the cells clump more easily. At higher cell concentrations, more cells clump, which leads to a decrease of inactivation rate by HPCD [52].

②Although cells are prone to clump under pressure, more severe shear force could be obtained from applying HPCD to separate cells. Therefore, higher pressure leads to a higher inactivation rate [47].

③Pressured CO_2 can cause cell surface damage and disruption to intracellular organization.Under scanning and transmission electron microscopes (SEM and TEM), the alteration of microbial cell morphology can be visualized, after HPCD treatment. These alterations can be enhanced by longer treatment times [66, 67]. A large number of bulges were found on the extracellular surface of HPCD-treated cells, which indicates the leakage of cytoplasmic contents. However, morphological alteration is not necessarily the reason for cell death, because inactivated cells can still seem to be integral, under the TEM [52].

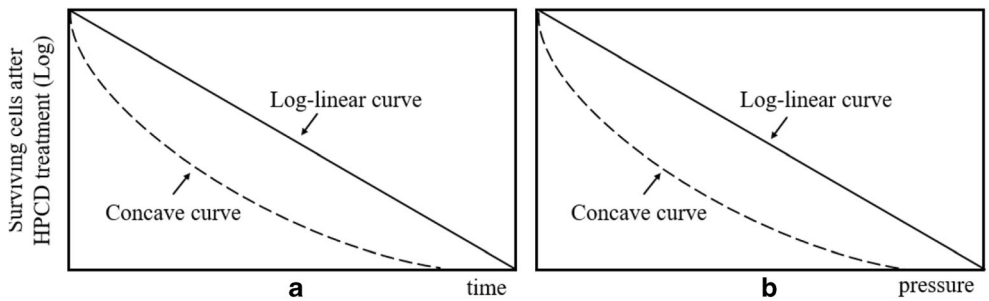

Fig. 3 Schematic representation of survival curve shapes (vegetative microbial cells) during HPCD inactivation (a so-called shoulder period was removed out of discussion in this paper). **a** Survival efficiency following time. **b** Survival efficiency following pressure

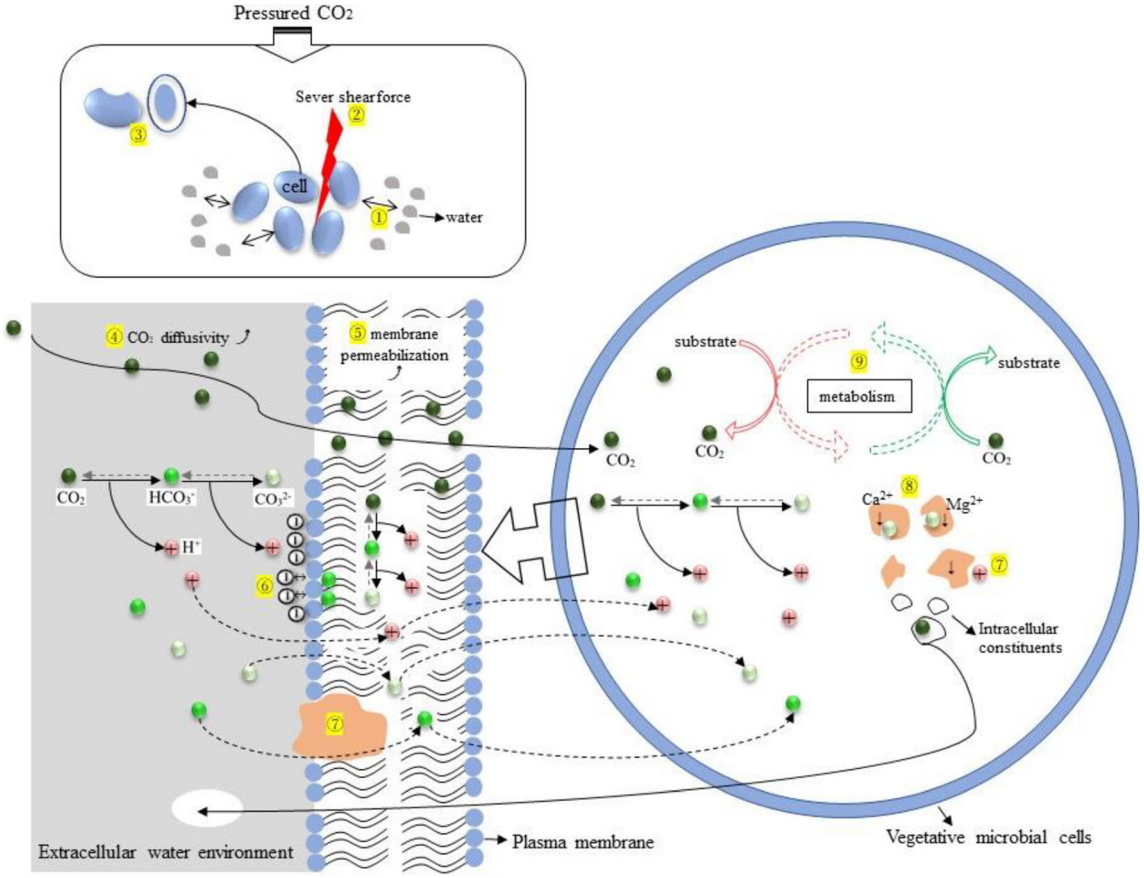

Fig. 4 Diagram of HPCD inactivation mechanisms on vegetative microbial cells

④CO_2 diffusivity is enhanced at high pressure and extracellular pH is decreased. Dissolved CO_2 can convert to HCO_3^- and CO_3^{2-}. Meanwhile, H^+ can be released from H_2O. In the aqueous extracellular environment, the pH will decrease due to release of H^+, which can also increase membrane permeabilization, to allow more CO_2 to enter the cytoplasm. This explains why the HPCD inactivation efficiency of dry strains was greatly decreased. However, regardless of the liquid matrix, the pH induced by the pressured CO_2 will not decrease constantly with pressure and temperature.

⑤Membrane permeabilization and fluidity are enhanced.About 81% of cells were permeabilized and 18% of cells were partially permeabilized after 15 min of CO_2 treatment under pressure (12 MPa and 35 °C). Additionally, the ratio of phosphoglyceride to phosphatidylethanolamine decreased, which indicated that the stability of the *E. coli* membrane also decreased under approximately 12 MPa of pressured CO_2 treatment [68]. This study confirmed the increase in cell membrane permeability and the leakage of intracellular cytoplasmic solutes which may be essential for microbial growth. Another research showed that HPCD can lead to a decrease in total saturated fatty acid content and an increase in total unsaturated fatty acid content [48]. Subsequently, the stability and permeabilization of cell membranes are altered. Membrane damage in a large majority of cells was also observed in the work of Fleury et al. [52]. Kobayashi et al. [49] also found that higher temperatures can increase the phase transition of the membrane, which may disrupt cytoplasmic membrane permeabilization. Another study also found that the disruption of the endoplasmic reticulum, nuclear membrane, Golgi body, and nucleolus caused a reduction in yeast cell viability when *Saccharomyces cerevisiae* was treated by HPCD. The membranes of major organelles were damaged by HPCD treatment, rather than the cell membrane [69]. Their investigation proved that membrane damage is also a lethal cause for eukaryotes.

⑥Decreased pH and HCO_3^- (produced from CO_2) in the membrane can destroy the membrane surface charge balance and alter membrane functions.The lower pH produced by pressured CO_2 may decrease the activity of some membrane proteins, and become deleterious to their biological functions. HCO_3^- ions produced by pressured CO_2 can change protein-lipid electrostatic interactions. For example, the topology of the inner membrane protein is believed to be influenced by the presence of negatively charged phospholipids [70], which may be changed by HCO_3^- ions. The localization of the charged amino acids in the membrane may also be influenced by HCO_3^- ions. It should be noted that the conformation and function of membrane proteins are related to the composition

and distribution of membrane lipids [71]. Hence, alteration of membrane protein activity may influence the composition and distribution of membrane lipids. This explanation was corroborated by a study of lipid A, which plays an important role in cell survival and is distributed in the periplasmic space [48]. However, more studies are needed on how HCO_3^- ions and decreased pH might influence the functioning of membrane proteins.Furthermore, there are many DNA-specific attachment sites on cell membranes. These are required for DNA replication and for the process of cell segmentation [72]. As we have accepted that cell membranes can be altered significantly by HPCD, the possible alteration of DNA-specific attachment sites should be taken into consideration. This might provide more evidence for the mechanisms of the bactericidal effect of HPCD, and is another avenue for future research.

⑦Some proteins and enzymes may lose their activities, due to HPCD treatment. The activity of Na+/K + -ATPase, the main enzyme that maintains the balance of various substances inside and outside of cells, has been shown to be significantly decreased by HPCD, especially under higher pressure and longer treatment times [48]. Alkaline phosphatase, a periplasmic enzyme, can also be deactivated at lower temperatures with HPCD than with thermal treatment alone [49]. However, the intracellular pH change brought about by pressured CO_2 is not a major contributor to lethality [46]. Decreased pH was considered as the reason for some protein deactivation. However, the latest research suggests that protein deactivation by HPCD is due to an "interfacial denaturation" mechanism. In their recent study, Monhemi and Dolatabadi [73] used a molecular dynamics simulation method to clarify the mechanism of HPCD inactivation of proteins and enzymes. They suggested that protein denaturation occurs at the CO_2/water interface in a HPCD pasteurization system. They found that hydrophobic regions in the protein cores were expanded upon arrival at the CO_2/water interface. First, when HPCD starts, proteins and enzymes become accessible to the CO_2/water interface. Pressurized micro-size CO_2 bubbles and mixing in the processing vessel can both promote this movement. Second, hydrophobic protein regions start to unfold, from globular to flat and extending, in conformation. Third, tertiary protein structure undergoes change, followed by protein denaturation. This may also cause functional alterations in the membrane.

⑧Internal ribosomes and CO_3^{2-} (produced from CO_2) induce intracellular precipitation. Anions such as CO_3^{2-} or HCO_3^- may precipitate intracellular inorganic electrolytes (Ca^{2+}), leading the cytoplasmic interior to lose its electrolytic balance. Subsequently, with increased permeability, these inorganic electrolytes and other constituents may transfer to the extracellular environment through the cell membrane. This has been confirmed by some studies. After HPCD treatment, an obvious increase was found in the types of protein in the supernatant, which indicated that the constituents of the cells were transferred to the extracellular space [48]. When intracellular constituents are removed, the structure of the biomembrane and the balance of the biological system may be altered, which could enhance the lethal effect of pressurized CO_2.In addition, internal ribosomes and intracellular materials can be agglomerated or precipitated, followed by uneven distribution at the cell membrane [48]. Precipitation of intracellular ribosomes can, subsequently, cause confusion in gene expression.

⑨The metabolic pathways that require CO_2 as a reagent can be stimulated. Those that can produce CO_2 will be inhibited. Phosphatidylcholine synthesis increases with pressurized CO_2 treatment. This can explain the enhanced stability of some cell membranes and cellular resistance to HPCD inactivation [67], as bacteria present enhanced adaptability to the adverse external environment. The metabolism of the urea cycle is also significantly enhanced, along with the induction of urea cycle-related genes [74]. These studies revealed that HPCD can influence cell metabolism.

Mechanism of HPCD Inactivation of Spores

Spores usually possess a high ability to resist physical and chemical treatment, due to their unique structure [75]. Spore structure includes an exosporium, a coat layer, outer membrane, cortex, germ cell wall, inner membrane, and core [76] (Fig. 5). The permeability barrier is composed of an exosporium, a coat layer, and a cortex that contributes to spore resistance against pressure or attack by chemicals and lytic enzymes [75].

Generally, spore inactivation by HPCD proceeds as follows. When heat is applied to spores, the enzymes in the spores may be activated, which may lead to cell modification. This provides an opportunity for CO_2 to penetrate the cell, followed by damage to the cell structure and metabolic systems. Subsequently, the fluidity and permeability of the inner membrane are increased by the HPCD. The evidence shows that HPCD treatment can trigger the loss of core materials from spores, such as metal ions and dipicolinic acid (DPA) from the inner membrane [77, 78]. Due to an increase in the permeability of the inner membrane, the heat resistance of the spore is also reduced by HPCD treatment. It should be noted that germination is not the reason that heat resistance of spores is reduced, as HPCD-treated spores did not undergo typical germination due to the damage of germinant receptors. Then, spore outgrowth is blocked due to the absence of germination, which leads to spore death [53, 78].

HPCD Inactivation on Food Enzymes

HPCD can promote the inactivation of enzymes. Especially in some fruits, vegetables, and some related products, peroxidase

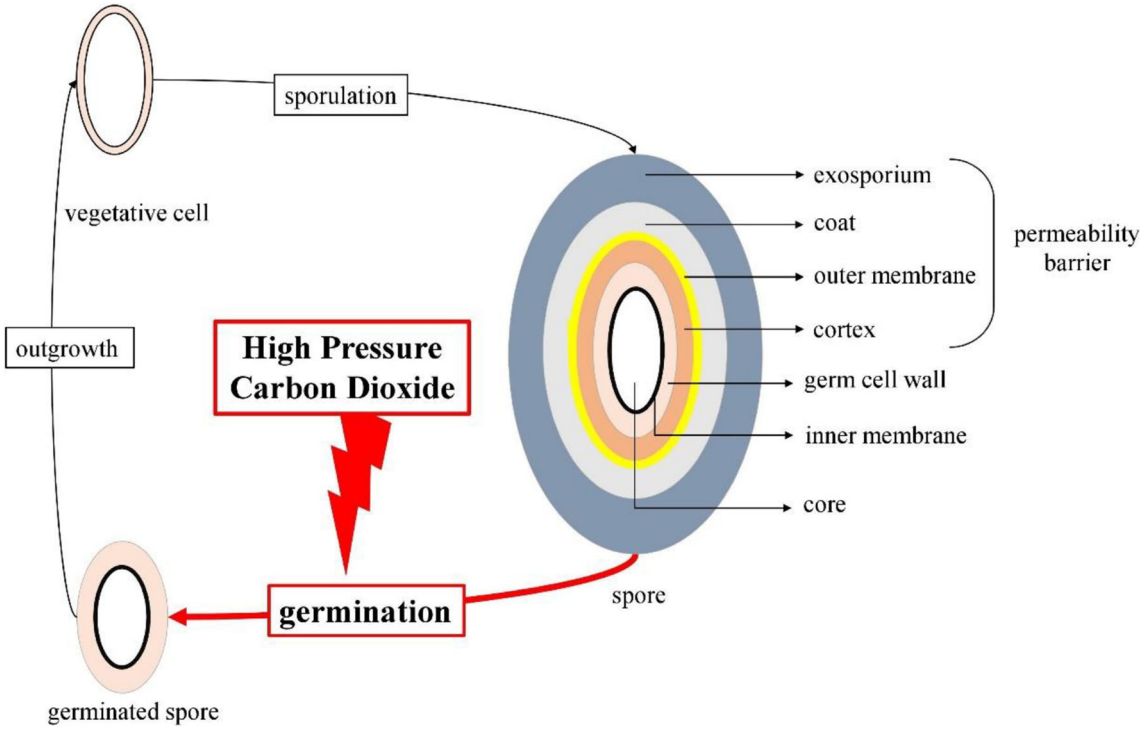

Fig. 5 Diagram of spore inactivation by HPCD

and polyphenol oxidase are the most important enzymes to negatively affect food quality by browning, the formation of off-flavors, and the loss of vitamins and pigments. The inactivation of peroxidase and polyphenol oxidase activity by HPCD is dependent on temperature, pressure, and time (Table 2). The remaining peroxidase activity was 61.39% after treatment with CO_2 at 20 MPa and 45 °C for 20 min, whereas, only 29.32% peroxidase activity was preserved when the temperature increased to 65 °C. Without HPCD, peroxidase activity remained at 94.56%, even when the temperature was increased to 65 °C [79]. When the CO_2 pressure increased to 30 MPa for 30 min, 83% of the peroxidase was effectively inactivated [47]. Compared with peroxidase, polyphenol oxidase is much more sensitive to HPCD treatment. HPCD conditions of 30 MPa and 45 °C for 30 min can totally inactivate polyphenol oxidase [47].

The CO_2 concentration is more important than the pressure, for inactivating enzymes. When 70% CO_2 was applied without pressure, 51% of protease was inactivated. When 150 MPa was applied, without CO_2, the inactivation was only 20%. The same results were obtained for collagenase activity. When 150 MPa pressure was applied with 100% CO_2, the inactivation of collagenase did not increase compared with 0 MPa pressure and 100% CO_2 treated collagenase (Table 2) [50]. Beside these examples, many other enzymes have been successfully inactivated by HPCD [80–86].

For a possible mechanism by which HPCD might inactivate enzymes, Benito-Román et al. [87] found, by fluorescence spectroscopy analysis, that HPCD can trigger significant changes in an enzyme's tertiary structure. Following this result, as previously mentioned, Monhemi and Dolatabadi [73] found that the tertiary structure of proteins and enzymes is significantly changed from globular to flat and extended conformations. The alteration of protein structure is considered to be the main cause of inactivation, and a more detailed description has been given in Section 4.1 (⑦).

The Influence of HPCD on Food Nutrition and Organoleptic Properties

Nutrition

As a kind of novel nonthermal pasteurization technology, the purpose of HPCD is to maintain more nutrition after pasteurization processing. Therefore, the influence of HPCD on food nutrition needs to be discussed. The effects of HPCD on nutritional value are summarized in Table 3 according to recent researches.

It was presented that, after HPCD treatment, the residual Ca^{2+} in the orange juice can keep at more than 90%. More Ca^{2+} loss cannot be caused by higher temperatures but can be caused by higher pressure and longer treatment time [88]. Same with residual Ca^{2+}, HPCD also induces a slight decrease in protein and lactose content [89].

Marszalek et al. [47] found that HPCD can enhance the sugar content. However, when the lower pressure, lower

Table 2 Inactivation of HPCD on enzymes. *CSF* (coho salmon fillets); *RT* (room temperature); *HHP* (high hydrostatic pressure)

Enzymes	Food species	Conditions	Additional technique	Results	Reference
Peroxidase	Strawberry juice	(30, 60 MPa), 45 °C, 30 min	No	83%, 88% inactivated	[47]
Peroxidase	Apple juice	20 min, 65 °C	No	5.44% inactivated	[79]
Peroxidase	Apple juice	20 MPa, 20 min, 45 °C	No	38.61% inactivated	[79]
Peroxidase	Apple juice	20 MPa, 20 min, 65 °C	No	70.68% inactivated	[79]
Polyphenol oxidase	Strawberry juice	(30, 60 MPa), 45 °C, 30 min	No	100% inactivated (both)	[47]
Polyphenol oxidase	Apple juice	20 MPa, 20 min, 45 °C	No	81.55% inactivated	[79]
Polyphenol oxidase	Apple juice	20 MPa, 20 min, 55 °C	No	100% inactivated	[79]
Protease	CSF	RT, 5 min, 0 MPa + 70% CO_2	HHP	51% inactivated	[50]
Protease	CSF	RT, 5 min, 150 MPa + 50% CO_2	HHP	20% inactivated	[50]
Protease	CSF	RT, 5 min, 150 MPa + 100% CO_2	HHP	59% inactivated	[50]
Collagenase	CSF	RT, 5 min, 0 MPa + 100% CO_2, 10 days storage	HHP	91% inactivated (compare with 0 MPa and 0% CO_2)	[50]
Collagenase	CSF	RT, 5 min, 150 MPa + 100% CO_2, 10 days storage	HHP	91% inactivated (compare with 0 MPa and 0% CO_2)	[50]

temperature, and less treatment time of HPCD was applied on inulin-enriched apple juice, HPCD treatment presented no big influence on sugar content [90].

For vitamin C, pressure makes little difference to the preserved content because 60 MPa can induce 33% loss, whereas 30 MPa induced 30% loss. However, due to pressure utilization, the temperature can be decreased. Temperature has a greater influence on vitamin degradation than pressure. When the temperature decreased from 45 to 38 °C, preserved vitamin C increased from 70 to 89%. Furthermore, more vitamin C can be preserved at lower HPCD temperatures with the help of ultrasound [45, 47, 52].

HPCD treatment of below 20 MPa made no big effects on organic acids, a kind of very important nutritional compounds with antioxidant activity in many fruits [90]. The phenolic compounds, which also possess antioxidant activity, are also not influenced greatly by HPCD treatment [79, 90]. However, Murtaza et al. [79] presented that higher temperatures can induce an even greater loss of phenolic content. Furthermore, when higher pressure and higher temperature (60 MPa, 55 °C) were applied, about 30% polyphenols were degraded [91].

Anthocyanins are protected during HPCD, since there is no reduction after 30 MPa 45 °C HPCD treatment for 30 min. When the pressure is increased to 60 MPa, the anthocyanin content only decreased by 3% [47]. Betaxanthins which contribute to plants color and possess antioxidant ability were also invested under HPCD treatment. It was found that higher temperature and higher pressure can both increase betaxanthins degradation. Especially when the pressure was increased to 60 MPa and the temperature increased to 55 °C for 30 min, 32.1% degradation of betaxanthins was detected [91]. Compared with betaxanthins, betacyanins seems much more sensitive to HPCD treatment.

In summary, despite betacyanins which are very sensitive to HPCD treatment, most nutritional compounds can only be degraded slightly by HPCD treatment. Therefore, HPCD can be used as a novel nonthermal pasteurization technology with low nutrition loss in the food industries. But according to these analyses that higher temperature and higher pressure can induce more nutrition degradation, lower pressure and lower temperature are recommended in the real industrial application.

Organoleptic Properties

To make the products more acceptable for consumers is also an essential task. Therefore, the organoleptic properties of HPCD-treated samples are discussed here. The influence of HPCD on food organoleptic properties has been summarized in Table 4.

Table 3 Influence of HPCD on food nutrition (1) and (2)

Nutrition	Food species	HPCD condition	Additional technique	Result	Reference
(1)					
Residual Ca^{2+}	Orange juice	10 MPa, (21, 40 °C), 20 min	No	91%, 96%	[88]
Residual Ca^{2+}	Orange juice	(10, 30 MPa), 40 °C, 20 min	No	96%, 93%	[88]
Residual Ca^{2+}	Orange juice	10 MPa, 40 °C, (20, 40 min)	No	96%, 90%	[88]
Protein content	Bovine milk	20 MPa, (20 ~ 50 °C), (20 ~ 70 min)	No	Slight loss	[89]
Lactose content	Bovine milk	20 MPa, (20 ~ 50 °C), (20 ~ 70 min)	No	Slight loss	[89]
Total sugars	Strawberry juice	45 °C, 30 min (30, 60 MPa)	No	6.6%, 7.7% increase	[47]
Total sugars	Inulin-enriched apple juice	(10, 15, 20 MPa), 35 °C, 10 min	No	No big influence (all)	[90]
Vitamin C	Mixture of plant extracts	(38, 50 °C), 10 MPa, 75 min	No	11% inhibition	[52]
Vitamin C	Pineapple juice	10 MPa, 31 °C, 3.06 min	Ultrasound	1.97% inhibition	[45]
Vitamin C	Strawberry juice	(30, 60 MPa), 45 °C, 30 min	No	30%, 33% inhibition	[47]
Organic acids present	Inulin-enriched apple juice	(10, 15, 20 MPa), 35 °C, 10 min	No	No big influence (all)	[90]
(2)					
Total phenolic compounds	Apple juice	20 MPa, 20 min, (25, 65 °C)	No	5.9%, 11.5% decreased	[79]
Total phenolic compounds	Inulin-enriched apple juice	(10, 15, 20 MPa), 35 °C, 10 min	No	No big influence (all)	[90]
Polyphenols	Beetroot juice	60 MPa, 55 °C, 30 min	No	30.7% degraded	[91]
Anthocyanins	Strawberry juice	(30, 60 MPa), 45 °C, 30 min	No	0%, 3% inactivated	[47]
Betaxanthins	Beetroot juice	60 MPa, (31, 39, 55 °C), 30 min	No	11.5%, 19.5%, 32.1% degraded	[91]
Betaxanthins	Beetroot juice	(10, 30, 60 MPa), 39 °C, 30 min	No	15.2%, 18.9%, 19.5% degraded	[91]
Betacyanins	Beetroot juice	60 MPa, (31, 39, 55 °C), 30 min	No	23.6%, 43.8%, 58.6% degraded	[91]
Betacyanins	Beetroot juice	(10, 30, 60 MPa), 39 °C, 30 min	No	38.7%, 39.9%, 43.8% degraded	[91]

Table 4 Inactivation of HPCD on food quality (1) and (2). *RCBM* (raw chicken breast meat); *CSF* (coho salmon fillets); *LESMM* (lyophilized equine skeletal muscle myoglobin); *RT* (room temperature); *HHP* (high hydrostatic pressure); ΔE (color change)—[not noticeable (0~0.5), slightly noticeable (0.5~1.5), noticeable (1.5~3), well visible (3.0~6.0), great (6.0~12.0)]

Features	Food species	HPCD condition	Additional technique	Result	Reference
(1)					
pH	Bovine milk	20 MPa, 20 °C, (20~70 min)	No	8.7~10.1% decreased (5.97~6.06)	[89]
pH	Bovine milk	20 MPa, (20~50 °C), 20 min	No	10.1~11.9% decreased (5.85~5.97)	[89]
pH	Apple juice	20 MPa, 20 min, (25, 65 °C)	No	2.5%, 11.4% decreased (3.58, 3.25)	[79]
pH	RCBM	(8, 14 MPa), 40 °C, 45 min	No	No big change (5.7~5.9)	[51]
pH	Inulin-enriched apple juice	(10, 15, 20 MPa), 35 °C, 10 min	No	No big influence (all)	[90]
pH	Strawberry juice	(30, 60 MPa), 45 °C, 30 min	No	3.33	[47]
pH	CSF	RT, 5 min, 150 MPa + 100% CO_2	HHP	6.41	[50]
Color	Apple juice	20 min, (25~65 °C)	No	ΔE (4.30~8.12)	[79]
Color	Apple juice	20 MPa, 20 min, (25~65 °C)	No	ΔE (7.2~14.54)	[79]
Color	Strawberry juice	(30, 60 MPa), 45 °C, 30 min	No	ΔE = 1.09, ΔE = 0.57	[47]
Color	Orange juice	30 MPa, 40 °C, 40 min	No	ΔE = 5.1	[88]
Color	CSF	RT, 5 min, 150 MPa + 0% CO_2	HHP	ΔE = 15.2	[50]
Color	CSF	RT, 5 min, 0 MPa + 70% CO_2	HHP	ΔE = 3.3	[50]
Color	CSF	RT, 5 min, 150 MPa + 50% CO_2	HHP	ΔE = 4.4	[50]
(2)					
Turbidity	Bovine milk	20 MPa, 20 °C, (20~70 min)	No	4.4~7.6% increased	[89]
Turbidity	Bovine milk	20 MPa, (20~50 °C), 20 min	No	4.4~21.9% increased	[89]
Average particle size	Bovine milk	20 MPa, 20 °C, (20~70 min)	No	0.3~49.1% increased	[89]
Average particle size	Bovine milk	20 MPa, (20~50 °C), 20 min	No	0.3~51.4% increased	[89]
Viscosity	Bovine milk	20 MPa, (20~50 °C), (20~70 min)	No	Slightly decrease (all)	[89]
Viscosity	Inulin-enriched apple juice	(10, 15, 20 MPa), 35 °C, 10 min	No	No big influence (all)	[90]
Total solids content	Bovine milk	20 MPa, 20 °C, (20~70 min)	No	4.9~6.4% decreased	[89]
Total solids content	Bovine milk	20 MPa, (20~50 °C), 20 min	No	4.9~12.5% decreased	[89]
Soluble solid content	Inulin-enriched apple juice	(10, 15, 20 MPa), 35 °C, 10 min	No	No big influence (all)	[90]
Hardness	RCBM	0~14 MPa, 40 °C, 45 min	No	145.4~85.2% increased	[51]
Springiness	RCBM	0~14 MPa, 40 °C, 45 min	No	No big changes	[51]
Gumminess	RCBM	0~14 MPa, 40 °C, 45 min	No	151.7~75.3% increased	[51]

It was found that the HPCD technique can reduce the concentrations of volatile compounds in foods, and may influence their aroma [92, 93].

The pH and titratable acidity contribute to food sourness, total soluble solids, and sweetness (fructose, glucose, and sucrose). Because of the complex food matrix, HPCD has no significant influence on food pH (Table 4). However, the pH varies greatly between different foods. The pH of strawberry juice and apple juice is always between 3 and 4 regardless of the pressure, temperature, and treatment time. Whereas, the pH of HPCD-treated chicken breast meat stays at around 5.7 and the pH of coho salmon fillets is 6.41 [47, 50, 51, 79]. However, HPCD can still induce a slight decrease in pH in apple juice. A higher pressure leads to a lower pH value, which indicates that higher pressure and temperature can trigger more CO_2 being dissolved into water [79].

The alteration of food color by HPCD was investigated. The yellowness varied in different food sources and by different HPCD treatment conditions. The degree of browning is decreased in apple juice, carrot juice, and hami melon juice [58, 94, 95]. In recent studies, total color differences were used to analyze food color changes. A higher temperature caused a greater alteration in food color, and HPCD can increase the color alteration, at the same temperature, in apple juice. However, there were no significant changes in color when the strawberry juice was treated with HPCD. An obvious color change in orange juice was also observed under 30 MPa, 40 °C for 40 min treatment. This suggests that the influence of HPCD on color varies between foods [47, 79, 88]. Another study demonstrated that, compared with CO_2, pressure had a greater influence on food color (Table 4). Perez-Won et al. [50] showed that, when pressure is applied without CO_2, large changes in color could be observed. However, there was less change in the color with CO_2 alone, without pressure treatment.

HPCD increases the cloudiness, average particle size, and viscosity of HPCD-treated juices, which can provide good juice quality for customers. For example, HPCD-treated orange juice presented an increased proportion of the smaller particles, which contributed to the juice cloud and stability, improving the juice quality. Furthermore, increased viscosity was observed in HPCD-treated peach juice [93, 96], but Silva et al. [90] observed that HPCD with relatively lower pressure and temperature made no big influence on the viscosity of inulin-enriched apple juice. The turbidity and average particle size of bovine milk can be increased by higher temperatures and longer treatment time, but HPCD can decrease the viscosity and total solids content of bovine milk, which is different from fruit juices [89].

For solid food, firmness of pear, hardness of carrot slices, and hardness of milled rice are all decreased after HPCD treatment [97–99]. When raw chicken breast meat was treated with HPCD, a decrease in gumminess and hardness was observed, with increasing pressure. In contrast, at higher pressure, springiness increased. However, it should be noted that the temperature can also increase gumminess and hardness, since a significant increase was found when the same temperature and treatment time was applied, without HPCD (Table 4) [51].

In summary, the many merits of HPCD treatment show that it is a good future choice as a nonthermal pasteurization technology, in the food industry. First, HPCD can effectively inactivate microorganisms and some food enzymes, which would negatively affect food quality and extrinsic features. Second, HPCD can provide products with a better appearance, which contributes to selling. Third, HPCD technology has a low requirement for equipment and cost, due to the application of relatively low temperatures and pressures.

However, our concern is that, except for some beverages with a lower initial pH, HPCD-treated products may influence the flavor, to some extent, because of decreased pH. Therefore, in real industrial applications, the influence of HPCD on different products taste should be taken into consideration. It should also be noted that HPCD technology cannot be applied to soft foods and leafy vegetables because the applied pressure and CO_2 may alter the food matrix and sensory characteristics, making food unacceptable for consumers.

Future Prospects and Conclusions

This review provides a simple introduction to existing pasteurization technologies in the food industry. The current state of knowledge, of HPCD pasteurization technology, has been explained. It has been confirmed that this process could be applied in the food industry as a novel, nonthermal pasteurization technology, since the bactericidal effect of HPCD has been widely tested on various microorganisms. Additionally, the influence of HPCD on food quality was considered. However, a lack of ample studies prevents HPCD technology from growing on an industrial scale. Although the inactivation of microorganisms by HPCD has been studied extensively, the detailed mechanisms are still unclear. Until now, studies have shown that the alteration of the cell membrane is the leading cause of bactericidal activity. Hence, in future works, scientists should give more consideration to membrane alteration by HPCD treatment, whose possible mechanisms we have introduced at length, in this review. To date, studies on the inactivation of spores and viruses by HPCD have been insufficient, especially on some food pathogens, such as *Clostridium* spores, which can cause spoilage, and foodborne illness. In addition, a further study of the mathematical modeling of the inactivation kinetics of various microorganisms should be conducted to provide data for industrial application.

More systematic and quantitative research on the influence of HPCD on food composition is needed, as this is essential for nutritive value, quality, and function, which directly

influence consumer desire. Although Hibi et al. [100] concluded that no toxic materials exist in HPCD-treated bread, more work investigating the safety of HPCD-treated food needs to be done, because HPCD is a new pasteurization technology.

To satisfy consumers' increasing demands for food safety and quality, HPCD can provide a solution. Owing to the lower requirement for pressure (lower than 50 MPa) compared with HHP technology, HPCD has great advantages, such as low cost in equipment, larger scale production, and is much safer for operators. In addition, CO_2 is cheap and is considered "green," in the context of food science, without toxicity. However, the process parameters (pressure, temperature, and treatment time) of HPCD for different foods need to be studied energetically. More efforts are needed to provide more convincing data for future, commercial-scale applications.

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