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Nonconventional Technologies in Lipid Modifications

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Abstract

Lipid modifications play a crucial role in various fields, including food science, pharmaceuticals, and biofuel production. Traditional methods for lipid modifications involve physical and chemical approaches or enzymatic reactions, which often have limitations in terms of specificity, efficiency, and environmental impact. In recent years, nonconventional technologies have emerged as promising alternatives for lipid modifications. This review provides a comprehensive overview of nonconventional technologies for lipid modifications, including high-pressure processing, pulsed electric fields, ultrasound, ozonation, and cold plasma technology. The principles, mechanisms, and advantages of these technologies are discussed, along with their applications in lipid modification processes. Additionally, the challenges and future perspectives of nonconventional technologies in lipid modifications are addressed, highlighting the potential and challenges for further advancements in this field. The integration of nonconventional technologies with traditional methods has the potential to revolutionize lipid modifications, enabling the development of novel lipid-based products with enhanced functional properties and improved sustainability profiles.

1. INTRODUCTION

Fats and oils are widely employed in the food, pharmaceutical, and cosmetic industries because of their physicochemical and functional properties. Their functionalities depend primarily on the fatty acid composition and structural aspects. Each fat and oil shows unique characteristics, particularly crystallization and melting behaviors, polymorphism, solid fat content, fatty acid composition, and fat-soluble phytonutrients as well as other properties. Most of the time, each individual lipid source in its native state fails to provide the desired functional requirements for product application. Consequently, various modification strategies have been adopted to tailor the functional and physicochemical properties of lipids. These include physical (blending and fractionation) and chemical (hydrogenation, interesterification, hydrolysis, and esterification) processing methods as well as enzymatic approaches. The latter stands out from an economical and environmental viewpoint, but the high cost of commercial enzymes limits its applications. Despite the widespread usage of these techniques, some conventional techniques may trigger unwanted chemical reactions and lead to the formation of carcinogenic compounds owing to the extreme operating conditions. This, therefore, urges researchers and industry professionals to search for better alternative methods.

In recent years, there has been growing interest in nonthermal processing treatments such as high-pressure processing (HPP), pulsed electric fields (PEF), ultrasound, ozonation, and cold plasma (CP) technology. These innovative technologies offer advantages, including low energy consumption and treatment of raw materials at ambient temperature for short durations. They are used mainly to assure food safety and quality through the inactivation of microorganisms while preserving the nutritional content of foods. More importantly, the formation of heat-induced toxic compounds is minimized with these processing techniques. Previous studies indicate that these emerging technologies have enormous potential as they could modify the structures and functionalities of fats and oils (Gao & Meng 2024, Pérez-Andrés et al. 2018, Thirumdas 2022, Zulkurnain et al. 2017). For instance, ultrasound technology is used to control the nucleation of the fat crystallization and structure the crystalline network through the cavitation effect contributed by ultrasonication (da Silva et al. 2019, 2020; da Silva & Martini 2019). CP treatment offers a promising way to produce partially hydrogenated oil while mitigating the formation of *trans*-fatty acids, albeit in trace amounts (Puprasit et al. 2022, Yepez & Keener 2016). Besides, HPP has the potential to induce phase transition of lipids and affects their melting and crystallization profiles (Zulkurnain et al. 2016). Other nonthermal processing techniques also exhibit positive impacts in modifying the lipid structure, as indicated in the previous research (Naliyadhara et al. 2022, Pérez-Andrés et al. 2018). However, the challenge lies in understanding their mechanisms as well as their processing parameters to practically optimize the properties and functions of lipids. As such, we aim to review these nonconventional processing technologies in lipid modification, specifically focusing on their operational mechanisms and designs. This review also identifies promising routes or processing parameters for further investigation. The review is structured as follows: Section 2 presents a concise introduction to conventional methods used in fat and oil processing, along with the primary challenges associated with these methods. Nonconventional processing approaches are covered in Section 3. Section 3.1 describes the working principles of the HPP method and its applications in altering the physicochemical properties of lipids. Section 3.2 provides an overview of the operational concepts in PEF technology and its potential applications. In Sections 3.3 and 3.4, the fundamentals of CP technique and ozonation, respectively, are discussed, along with their effects on the characteristics and molecular structures of lipids, and Section 3.5 outlines the working mechanisms of the ultrasound technique and its practical applications. Finally, the review is summarized and concluded in Section 4, where the potential of these technologies is compared and suggestions for future research projects are provided.

2. CONVENTIONAL TECHNOLOGIES

Fats and oils play an important role in the sensory and texture development of food in addition to providing energy and nutritional value. However, the physicochemical and functional characteristics of fats and oils vary depending on their sources, primarily because of differences in chemical composition and profile. These variations often impose limitations on their applications within the food industry. To overcome the limitations, several conventional modification techniques have been developed, encompassing physical, chemical, and enzymatic methods (Jin et al. 2021, Lai et al. 2012, Lee & Wang 2022, Sivakanthan & Madhujith 2020, Vázquez & Akoh 2010, Willett & Akoh 2018, Zhang et al. 2021, Zhong et al. 2013). In this section, we highlight these modification techniques, elucidating their underlying mechanisms of action and examining the parameters that influence their effectiveness.

Blending and fractionation are common physical techniques employed for modifying fats and oils. Blending is a simple and cost-effective approach that involves the combination of two or more different types of oils with unique properties to create a new oil blend with desired characteristics without changing their chemical compositions (Chen et al. 2022; Hashempour-Baltork et al. 2016; Lai et al. 1999; Ng et al. 2014, 2021; Ong et al. 2019; Saberi et al. 2012). There has been extensive literature reviewing the impact of vegetable oil blending on physicochemical and nutritional properties as well as its applications in the food industry (Hashempour-Baltork et al. 2016, Sharma et al. 2023). This method produces blended oils with enhanced oxidative stability and shelf life, accompanied by improved flavor profiles and nutritional attributes. Studies have demonstrated improved oxidative stability in oil blends containing palm olein. For instance, a 50:50 blend of cottonseed and palm olein oils exhibited a significantly lower increase in polymeric compound content after 10 hours of frying compared to pure cottonseed oil (Arslan et al. 2017). Another study also indicated that the incorporation of palm olein, which contains high levels of palmitic and oleic acids, can enhance the stability of the oil blends owing to the high oxidative resistance of these fatty acids at elevated temperatures (Alireza et al. 2010). Physical blending also produces oil blends with balanced fatty acid profiles, which may offer potential benefits for cardiovascular health and other aspects of human health. However, the challenges of physical blending include compatibility of the oils and possible phase separation during storage. Achieving a homogeneous blend with consistent properties is the key consideration in this process.

Fractionation is another useful technique that aims to separate lipids into two fractions, namely stearin (solid fraction) and olein (liquid fraction), using a thermo-mechanical separation process. Fats and oils are complex mixtures consisting of various triacylglycerol molecules with distinctive physical and chemical properties. These components can therefore be separated according to their solubility and melting or crystallization points. The common fractionation technique includes dry fractionation, solvent fractionation, and detergent fractionation. Dry fractionation involves controlled cooling to induce crystallization of specific triacylglycerol components (saturated fractions), followed by separation from the liquid oil through filtration. Dry fractionation is a cost-effective, easy to operate, and environmentally friendly technique commonly used in palm oil refineries to produce olein and stearin fractions with specific physicochemical and functional properties (Calliauw et al. 2007, Lee & Wang 2022, Tong et al. 2021). Recent studies have shown the applicability of dry fractionation to various novel oil types such as high-oleic high-stearic sunflower oil (Bootello et al. 2011), macauba kernel oil (Magalhães et al. 2020), basa catfish oil (Zou et al. 2016), and palm-based diacylglycerol oil (Ab Latip et al. 2013). Gupta (2017) has identified several critical points that are important for achieving efficient processing and obtaining desirable properties in the end products. These factors include initial oil temperature, precrystallization, cooling rate, crystallization time, agitation, final crystallization temperature, and separation/filtration (Gupta 2017). On the other hand, solvent fractionation utilizes organic solvents such as acetone or ethanol to dissolve the specific lipid fractions at controlled temperatures, which are then separated from the remaining oil through filtration and distillation. The addition of solvents to the oil reduces the viscosity of the mixture, facilitating faster crystallization and resulting in purer and homogeneous fractions. The rapid crystallization process reduces the probability of cocrystal formation and dislocation within the crystal lattice (Bootello et al. 2015). The efficiency of the solvent fractionation process relies on several factors such as the selection of solvent, the ratio of oil to solvent, and the crystallization temperature (Lee & Wang 2022). Detergent (wet) fractionation involves the separation of the crystallized phase from the liquid with the aid of an aqueous solution containing a detergent (wetting agent; sodium lauryl sulfate) and an electrolyte (magnesium or sodium sulfate). The electrolyte agglomerates the oil droplets formed during the mixing process, whereas the detergent wets the surface of stearin crystals and displaces the entrained olein (Huey et al. 2015). Detergent fractionation has not received much attention owing to its possible detergent contamination in the end-product and high production cost (Kellens et al. 2007). Fractionation obtains lipid fractions with distinctive functional properties, thereby allowing the customization of specific food applications with enhanced texture, sensory attributes, and nutritional profiles.

Chemical modification methods alter the properties of lipids by changing their molecular structure through chemical reactions, including hydrogenation, interesterification, esterification, and hydrolysis in the presence of chemical catalysts. Hydrogenation involves the addition of hydrogen gas to unsaturated fatty acid chains under high temperatures (150–225°C) and pressures (2–5 atm) (Hastert 1981). However, partial hydrogenation may lead to the formation of *trans*-fat with adverse health effects. Interesterification rearranges the fatty acids on the glycerol backbone of triacylglycerol molecules (Ai et al. 2023, Lee et al. 2015), whereas esterification combines free fatty acids and glycerol to form acylglycerol and water (Lo et al. 2007, Norlelawati et al. 2012). Hydrolysis removes acyl groups from triacylglycerol molecules (Cheong et al. 2007; Phuah et al. 2012, 2016), and glycerolysis involves the migration of fatty acyl moiety from triacylglycerol molecules (edible oil) to the acyl acceptor (glycerol) (Lee et al. 2007). These chemical approaches lack reaction specificity and often yield unwanted by-products as a consequence of harsh operating conditions. Alternatively, the use of lipase enzymes offers a more promising approach with higher specificity, milder conditions, and reduced production of unwanted by-products (Kim & Akoh 2015; Lai et al. 2012, 2019; Phuah et al. 2015; Şahin-Yeşilçubuk & Akoh 2017). Nevertheless, the major drawback associated with this enzymatic approach is the high enzyme cost. It is worth mentioning that these methods can be synergistically employed to achieve the desired modifications in lipids for targeted applications. In summary, each of these conventional lipid modification techniques has its own advantages and disadvantages that depend on the specific application.

3. NONCONVENTIONAL TECHNOLOGIES

3.1. High-Pressure Processing

As one of the nonthermal food preservation techniques that have gained increasing interest in the food industries, HPP works on the principle of subjecting food to high pressure (400–600 MPa) under cooled or mild temperatures. Its main goal is to achieve the inactivation of harmful microorganisms, thereby sterilizing the food and extending its shelf life while still preserving the sensory, textural, and nutritional properties of food products (Yordanov & Angelova 2010). HPP operates by applying an instantaneous and uniform pressure to the food, either directly or indirectly via a pressurizing medium (commonly water) or insulated flexible containers. According to Le Chatelier's principle, the pressure increase shifts the system to attain the lowest volume. Like heat, the exertion of pressure resulted in phase changes, alteration in molecular arrangement, and changes in the chemical reactions. In HPP, food is subjected to high pressure for a short period (3–5 min) before the pressure is released and decompression occurs. The compression, holding, and decompression steps can be repeated for a few cycles, and the process is usually accompanied by increments and decrements in temperatures.

Despite recent attention to HPP as one of the novel food preservation methods, its application has been explicitly extended to fat and oil processing as a novel modification approach to altering the physical properties of fats and oils (triolein, trilaurin, diacylglycerol oil, oleic acid, linoleic acid, soybean oil, rapeseed oil, coconut oil, cocoa butter, and various types of emulsions) through accelerating lipid crystallization, increasing its melting points and leading to the changes to its density, viscosity, thermal conductivity, and specific heat (Zulkurnain et al. 2016). The method has shown promising results in transforming these lipid materials, paving the way for innovative applications in the food industry.

When subjected to high pressure, the structure of the lipid can be fine-tuned relatively easily because of weak van der Waals forces. Pressure alters the interatomic distance between molecules, leading to a nonlinear phase transition from liquid to solid and facilitating the reorganization of the molecules. Crystallization performed under HPP provides unique features not commonly seen in conventional cooling under atmospheric conditions, where the inclusion of pressure enhances the nucleation rate, affects the fat crystal shapes and sizes, and affects the polymorphism of fat crystals, which indirectly influence the fat crystallization network structure. These changes have significant implications for confectionery and baked products, such as chocolate and margarine, and lipid coatings, where the physicochemical attributes heavily rely on the fat crystal network. The application of HPP technologies proved to provide additional advantages in fat and oil processing, which include (*a*) accelerating the crystallization of fat crystals, thereby shortening the crystallization time during manufacturing, (*b*) enhancing the formation of the stable polymorphism of fat crystals and preventing the postcrystallization processes that can lead to hardening and blooming, and (*c*) producing small fat crystals resulting in smooth and delicate texture in the final product (Zulkurnain et al. 2016). Additionally, modifying the physical properties of fats and oils via HPP can act as an alternative for the preparation of *trans*-fat. This becomes particularly relevant following the banning of *trans*-fat by the Food and Drug Administration (FDA). The effectiveness and benefits of HPP have been demonstrated in the production of chocolate and plastic fat, showcasing a significant enhancement in the physical attributes of these products. Additionally, the application of HPP has been found to reduce processing time and lower energy consumption, making it a favorable choice for manufacturers aiming to optimize their production process.

As mentioned above, the primary processing of HPP involves compression, holding, and decompression. The processing conditions such as holding time, magnitude and rate of compression, and cycles of compression, holding, and decompression, as well as lipid composition, can have significant impacts on the thermophysical properties of fats and oils (Zulkurnain et al. 2016). For instance, (*a*) the crystallization is enhanced with the increase in the pressure magnitude, (*b*) single-step pressurization induces the rate of fat crystallization and produces a less stable crystal that is further transformed into a more stable polymorph upon decompression, and (*c*) multistep crystallization slowly induces nucleation and growth of crystals, leading to the formation of more stable fat crystals (Ferstl et al. 2011, Tefelski et al. 2008). In a study by Zulkurnain et al. (2016), it was found that a single compression with 10 min holding time using HPP resulted in a significant improvement in the textural properties of the binary mixture of fully hydrogenated soybean oil and soybean oil compared to atmospheric crystallization for 30 min. This highlights the importance of controlling the HPP conditions to achieve the desirable attributes of the modified fats and oils.

On the other hand, HPP has its downsides. Several studies have associated HPP with lipid oxidation, which is undesirable, as it negatively affects the food product quality and has deleterious effects on human health. The pressure exerted during HPP is believed to accelerate the formation of the covalent bonds in the propagation steps of lipid oxidation. A concise review was performed on the effect of HPP on lipid oxidation (Medina-Meza et al. 2014). When high-pressure-treated food samples such as yak fat, raw chevon, black tiger shrimp, and dry-cured ham were stored for specific periods of time (a week to 6 months), they exhibited higher levels of lipid oxidation than the control without HPP. However, other studies demonstrated the opposite result, showing that HPP had no significant impact on lipid oxidation. The discrepancy could be attributed to varied HPP processing conditions and the composition of the food (Fuentes et al. 2014, Jalarama Reddy et al. 2015, Kim et al. 2018, Lemus-Mondaca et al. 2018).

As HPP involves no chemicals or solvents and hastens the crystallization processing, the resulting product obtained can be regarded as "clean label" and aligns well with the demand for sustainable food production and the current focus on achieving sustainable development goals. Despite its apparent advantages, applying HPP in large-scale product manufacturing remains a challenge. One of the main challenges is the high operational cost of HPP compared to other conventional approaches used to improve lipid crystallization, such as tempering or seeding and additive addition. Using HPP solely for crystallization may seem unreasonable unless it serves multiple functionalities such as destroying the microorganism and inactivating lipase that could cause rancidity and off-flavors in oils while simultaneously improving lipid crystallization and product quality.

3.2. Pulsed Electric Field Processing

PEF processing was introduced in the late 1990s as a nonthermal food preservation technique aimed at extending the shelf life of food products through microorganism inactivation. This is achieved by applying high voltage (ranging from 10–80 kV) and short electric pulses (from microseconds to milliseconds) while subjecting the food to low and moderate temperatures (Puértolas et al. 2013). In PEF technologies, a food sample, whether liquid or semisolid, is placed between the two electrodes in a chamber that carries electric waves in various forms such as a decaying, square wave, bipolar, or oscillatory pulse over a short period. The total treatment time is determined by the multiplication of pulse intensity and pulse time. When exposed to high electric pulses, cell membranes generate pores by either enlarging existing ones or forming new ones, which can be either permanent or temporary. PEF processing is commonly used in the treatment of milk and juices to achieve microbial inactivation (Huang & Wang 2009). Beyond its application in microbial inactivation, the use of PEF processing application has extended to the extraction of components embedded in the intracellular matrix of the cells when pulses help to enhance the extraction yield (Ranjha et al. 2021).

In fat and oil applications, PEF has also garnered particularly significant attention for enhancing the extraction of valuable lipophilic components and increasing extraction yield. Unlike conventional extraction techniques, PEF provides an additional advantage whereby the mild conditions protect the valuable components from degradation. For instance, PEF has been used as an assisted technology to extract oil from various sources such as cannabis, rapeseed, black cumin, Pacific white shrimp, microalgae, and sunflower to name a few (Bakhshabadi et al. 2018, Guderjan et al. 2007, Haji-Moradkhani et al. 2019, Shorstkii et al. 2020, Silve et al. 2018). Nevertheless, so far, no studies have utilized PEF for the physical and chemical modification of the fats and oils to confer them with new physicochemical attributes such as new melting and thermal properties, etc. One plausible explanation is that, unlike water, fats and oils have relatively low electrical conductivity. In most cases, PEF has been reported to lead to the formation of lipid-oxidized components because of the electrochemical changes introduced during the processing, which may eventually result in the production of toxic chemicals such as oxygen, peroxide, hydroxyl radicals, and chloride ions. Consequently, most studies focus on the side effects of PEF on product quality. Pérez-Andrés and his team conducted a concise review of the impact of PEF on lipid oxidation (Pérez-Andrés et al. 2018). They found that products subjected to PEF were more prone to oxidation during storage than those not treated with PEF. This evidence was supported by the degradation of the quality of chilled and frozen lamb and beef products, where certain fatty acids were converted into oxidized products (Faridnia et al. 2015, Ma et al. 2016). However, a few studies reported that PEF either retards or has no significant effect on oxidation of the frozen beef (Arroyo et al. 2015). These discrepancies are attributed to the divergent processing conditions used such as frequency, pulses, and voltages.

In another circumstance, PEF was employed to intensify an enzymatically catalyzed reaction by altering the lipase's orientation and reducing mass transfer limitation to a lesser extent. However, it is essential to note that excessive use of a high electric pulse may lead to lower conversion yield owing to the inactivation of the enzyme lipase. In the case of lipase-catalyzed hydrolysis of triacylglycerol, PEF was shown to enhance the reaction rate. For instance, in the stirred tank batch reactor, when subjected to PEF of 60 V, the lipase-catalyzed hydrolysis reaction exhibited up to 40% improvement in conversion at 24 h compared to the reaction performed without PEF (Anand et al. 2021).

At present, the application of PEF to fat and oil modification, in particular vegetable oils, remains rare and limited. However, it is essential not to overlook the potential of PEF on other fat and oil food systems, e.g., emulsion. As mentioned above, the principal obstacles to its utilization are mainly attributed to the inherent nature of the fats and oils, which have low conductivities and dielectric constants. To address this, studies can be performed to investigate the effects of adding water to fat and oil systems when applying PEF treatment. However, it is important to note that adding water to the fat and oil systems may only be feasible for some food applications. Nonetheless, it could be more practical in food emulsion. Additionally, it is also worth considering the disadvantages associated with PEF. One particular concern is the potential leaching of metals from the electrodes to the food samples. European legislation has already set the tolerable limit for the amount of metal permitted in food samples (Roodenburg 2007). Therefore, it is crucial to carefully address and monitor this issue to ensure compliance with safety standards.

3.3. Cold Plasma Technology

CP technology has attracted a lot of attention recently, particularly from the agri-food industry, owing to its high efficiency, environmentally friendly nature, and absence of chemical residues. CP is a type of nonthermal plasma that is created by applying sufficient energy (electromagnetic or electric fields, microwave, and radio frequencies as energy sources) to a gas, for example, helium, argon, hydrogen, and others, at ambient or low pressure. This process results in the formation of various reactive species such as ions, electrons, free radicals, and other substances (Moreau et al. 2008, Thirumdas 2022). It is interesting to note that although the temperature of the plasma electrons is high (several thousand Kelvin), the temperature of the positive ions and neutral particles in the plasma is relatively low (close to room temperature) owing to the lack of local thermodynamic equilibrium. This leads to the generation of an ionized gas system with a low-temperature characteristic (Okyere et al. 2022, Thirumdas 2022). The low-temperature profile of the resulting plasma makes it suitable for a wide range of applications. One potential application of CP technology is modifying the lipid composition, which indirectly alters the physicochemical properties of lipids.

Hydrogenation is a chemical process that involves the addition of hydrogen molecules to liquid oil, typically rich in unsaturated fatty acids, in the presence of a chemical catalyst (such as nickel or palladium) at extreme operating conditions to produce solid fat. Unfortunately, the use of a chemical catalyst coupled with high temperatures can result in the formation of *trans*-fatty acids as an undesired by-product. Numerous studies have demonstrated clear evidence of the positive correlation between these *trans*-fats and a heightened risk of heart disease and other related complications (Islam et al. 2019, Oteng & Kersten 2019, WHO 2018).

The recent disclosure of CP hydrogenation presents a promising alternative to produce saturated fats while mitigating the formation of *trans*-fat. This innovative technology operates by generating hydrogen radicals or ions through the ionization of hydrogen gas molecules. These highly reactive species interact with unsaturated fats, leading to the conversion of double bonds into saturated fatty acids. It is worth noting that the addition of a single hydrogen atom to the double bond may generate a carbon-centered radical, which has the potential to form *trans*-fats. However, the production of *trans*-fats is minimal in CP hydrogenation. This is attributed to the unique characteristics of CP technology, which avoids the absorption/desorption process of reactants on the catalyst surface commonly found in traditional catalytic hydrogenation methods. The absence of this process helps circumvent the formation of harmful *trans*-isomers (Dijkstra 2006). Additionally, the low-temperature nature of the technology prevents isomerization and the development of *trans*-isomers, making it a desirable method for the hydrogenation of vegetable oil.

The effectiveness of CP hydrogenation relies on several factors, including gas composition, gas flow rate, types of oil, reaction conditions, reactor configuration, and others (Puprasit et al. 2020, Wongjaikham et al. 2022, Yepez 2020, Yepez et al. 2021, Yepez & Keener 2016). The choice and optimization of these parameters are important in achieving the desired final products. **Table 1** presents the important parameters to be considered for CP hydrogenation, along with their corresponding results. Gas composition is a crucial parameter that significantly affects the hydrogenation rate and quality of the final product. Previous studies investigated the hydrogenation of palm olein using dielectric barrier discharge (DBD) plasma with a needle-in-tube configuration system. The authors showed that increasing the hydrogen concentration could significantly enhance the hydrogenation rate (Puprasit et al. 2022). A similar observation was also reported by Yepez et al. (2021) in high-voltage atmospheric CP-exposed soybean oil, where a shorter time of approximately 4 h was needed to achieve an iodine value (IV) of 92 using pure hydrogen gas compared to the hydrogen–nitrogen (5%:95%) gas mixture, indicating the effectiveness of pure hydrogen gas in CP hydrogenation. However, the use of pure hydrogen gas for CP hydrogenation may lead to a minor formation of *trans*-fat (<3%) compared to a nitrogen–hydrogen gas mixture, attributed to the higher hydrogen concentration at equivalent pressures (Yepez et al. 2021). Besides, the design of a CP reactor may have an impact on the efficiency of the

Table 1 Key parameters and their corresponding results for cold plasma hydrogenation

Optimal operation parameters	Results	Reference
■ Reactor configuration: DBD plasma with needle-in-tube ■ Oil sample: palm olein ■ Gas composition: 100% H_2 ■ Gas flow rate: 0.5 L/min ■ Input power: 40 W ■ Gap distance: 0.5 cm between needle and oil ■ Reaction time: 15 h	■ IV: 23.56–60.75 g I_2/100 g ■ SFA composition: 40.82–68.70% ■ UFA composition: 31.39–59.11% ■ No TF ■ SMP: 9.33 ± 0.5–36.33 ± 0.5°C	Puprasit et al. 2022
■ Reactor configuration: microwave plasma with needle-in-tube ■ Oil sample: palm oil ■ Gas composition: 100% H_2 ■ Gas flow rate: 4 L/min ■ Input power: 600 W ■ Reaction time: 4 h ■ Temperature: 32°C (due to self-heating of the plasma) ■ Voltage: 60 kV	■ IV: 32.5–57.7 g I_2/100 g ■ TF: 4.23% ■ Good texture and SMP	Wongjaikham et al. 2022
■ Reactor configuration: DBD plasma with parallel plates ■ Oil sample: soybean oil ■ Gas composition: 5% H_2 and 95% N_2 ■ Input power: 200 W ■ Reaction time: 12 h ■ Temperature: 60°C	■ IV: 92–133 g I_2/100 g ■ No TF	Yepez & Keener 2016
■ Reactor configuration: DBD plasma with parallel plates ■ Oil sample: soybean oil ■ Gas composition: 100% H_2 ■ Reaction time: 6 h ■ Voltage: 80 kV	Solid fraction ■ IV: 86.6 g I_2/100 g (calculated) ■ TF: 2.8% ■ SFA composition: 16.7–22.5% ■ UFA composition: 21.6–61.7% ■ PC was detected	Yepez et al. 2021
■ Reactor configuration: DBD plasma with parallel plates ■ Oil sample: palm oil ■ Gas composition: 15% H_2 and 85% He ■ Gas flow rate: 0.8 L/min ■ Reaction time: 4 h ■ Temperature: 50°C (due to self-heating of the plasma) ■ Voltage: 10 kV	■ IV: 48.4–60.9 g I_2/100 g ■ SFA composition: 40.7 to 46.0% ■ UFA composition: 53.25–57.3% ■ TF: 1.44% ■ SMP increased at a rate of 2.2°C/h	Puprasit et al. 2020
■ Reactor configuration: RF-DBD plasma with parallel plates ■ Oil sample: oil extracted from plasma treated chia flour ■ Gas composition: atmospheric air ■ Input power: 60 W ■ Reaction time: 15 min	■ SFA composition: 11.4–16.6% ■ UFA composition: 81.0–87.0%	Upadhyay et al. 2019

Abbreviations: DBD, dielectric barrier discharge; IV, iodine value; PC, polymerized compounds; RF, radio frequency; SFA, saturated fatty acid; SMP, slip melting point; TF, *trans*-fat; UFA, unsaturated fatty acid.

hydrogenation process. Puprasit and coworkers (2022) conducted a study on the effects of various reactor parameters, including input power, gas flow rate, and discharge gap size, in a DBD system on the physicochemical properties and fatty acid profile of hydrogenated palm olein. Their findings indicated that optimizing these parameters (0.5 L/min gas flow rate, 40 W input power, 0.5 cm gap size) reduced the IV by 60% and increased saturated fatty acids by 70% after 15 h of treatment time (**Table 1**). Furthermore, the utilization of DBD plasma with the needle-in-tube configuration facilitates the bubbling of oil samples, thereby increasing the probability of contact between hydrogen reactive species and unsaturated fatty acids. Besides that, the CP hydrogenation process can be influenced by various reaction conditions, including residence time, moisture content, temperature, oil composition, and other related parameters. For example, Yepez (2020) demonstrated that the presence of moisture content can serve as a hydrogen source for CP hydrogenation, as evidenced by the decrease in IV and unsaturated fatty acids, despite the use of pure argon gas during the hydrogenation of soybean oil. It is important to note that CP may also trigger the formation of hydroxyl radicals from the moisture, which can potentially initiate lipid peroxidation reactions. Consequently, it is crucial to carefully monitor the CP process to minimize the generation of unwanted hydroxyl radicals and ensure product quality. Furthermore, a study by Puprasit et al. (2020) revealed that the optimal hydrogenation rate in DBD plasma-exposed palm oil occurred at an operating temperature of 50°C. Higher temperature is not recommended because of the exothermic nature of the hydrogenation process (Puprasit et al. 2020).

Although CP offers some advantages over conventional chemical methods, there are still several challenges that need to be addressed before this technique becomes feasible. An issue that arises is the occurrence of unwanted side reactions such as polymerization and oxidation, which were observed in previous studies (Yepez et al. 2021, Yepez & Keener 2016). Therefore, optimizing various operational parameters, including gas composition, moisture content, plasma power, temperature, reaction time, and other factors, is important in attaining optimal hydrogenation efficiency. In addition, scaling up CP hydrogenation operations for commercial applications may pose challenges in terms of reactor design, energy efficiency, and cost. Upon examining the CP mechanism, we believe that CP technology could be employed for other lipid modifications such as inducing intermolecular rearrangement of lipid molecules and forming partial acylglycerols. However, further research is needed to investigate the potential applications in greater depth and detail.

3.4. Ozonation

Ozone, which is a triatomic form of oxygen, has been widely used in the food industry for various applications, including disinfection and preservation, owing to its potent oxidative properties. Numerous studies in literature have demonstrated that ozone, owing to its high reactivity, has the potential to modify the chemical structure of lipids through ozonolysis. Criegee (1975) provided the first description of the mechanism behind the ozonolysis reaction (**Figure 1**). Ozonolysis involves the cleavage of a carbon–carbon double bond of unsaturated fatty acid ester in triacylglycerols, leading to the formation of a short-lived primary ozonide (molozonide). The unstable ozonide then decomposes into carbonyl oxide and carbonyl compounds, which further undergo a series of reactions, resulting in the production of diverse stable compounds (acids, aldehydes, secondary ozonides, α-hydroxyalkyl peroxides, and diperoxides), which can vary based on the presence of protic solvents (Criegee 1975, de Oliveira et al. 2017, Ugazio et al. 2020). Ozonolysis of fats and oils induces changes in their physicochemical properties such as melting and crystallization points, viscosity, and emulsifying properties, thereby affecting their functional characteristics (Ugazio et al. 2020). The control of ozonolysis is challenging because of the complexity of the reaction process. The difficulty lies in precisely regulating reaction parameters to achieve desired product profiles. Despite these challenges, ozonolysis holds potential for practical applications in modifying the physicochemical properties of fats and oils. Through further research and optimization, it may be possible to develop strategies to better control the process and manipulate

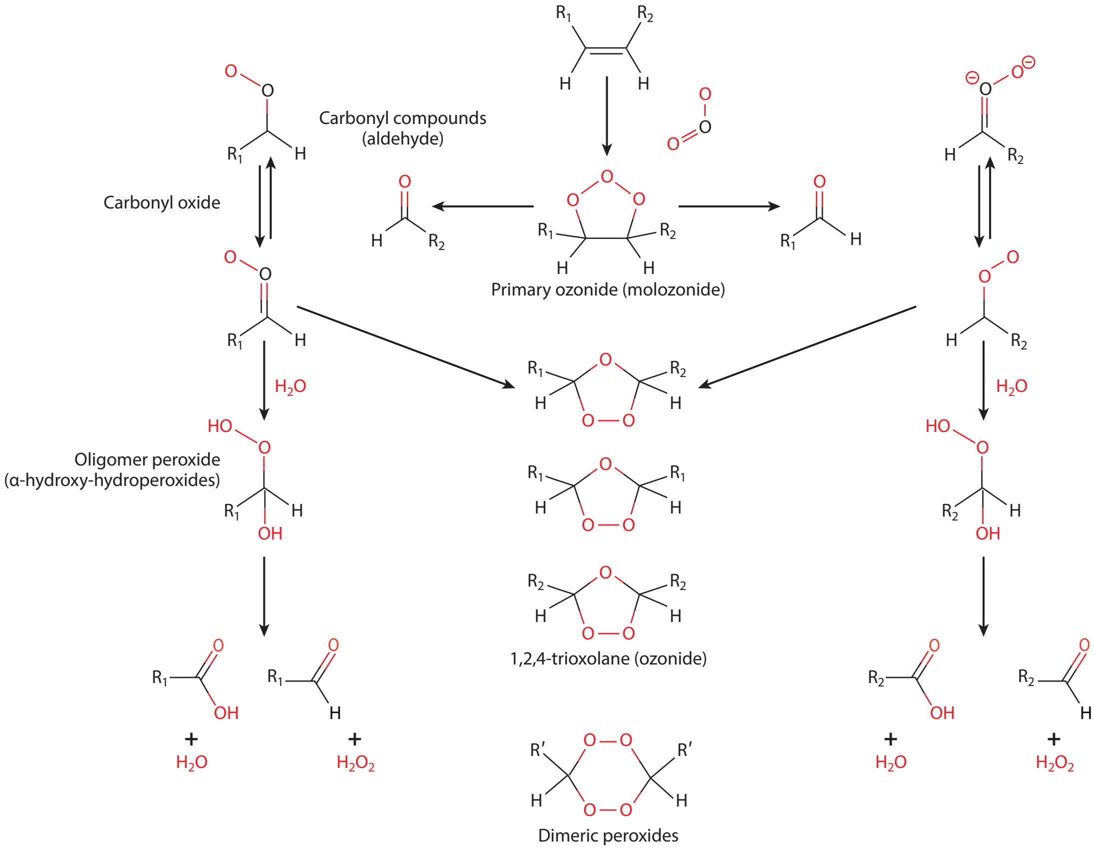

Figure 1

Criegee mechanisms. A three-step sequential reaction involving (*a*) the addition of ozone to the double bond of edible oil to form unstable primary ozonide (molozonide) and (*b*) subsequent dissociation into carbonyl compound and carbonyl oxide, after which (*c*) recombination occurs to form a more stable 1,2,4-trioxolane (ozonide) in the absence of protic solvent or generation of α-hydroxyalkyl peroxides in the presence of protic solvent.

product profiles to meet specific requirements in various industries such as food, pharmaceuticals, and cosmetics.

Ozone-treated oils (ozonated oils) have become increasingly popular in the food, pharmaceutical, and cosmetic industries because of their potential antimicrobial properties. The therapeutic antimicrobial effects of ozonated vegetable oils are believed to be a result of reactive oxygen species like ozonides and peroxides, which can damage and destabilize the cell membranes, leading to the destruction of microorganisms (Elisabetta et al. 2018). Apart from that, several studies demonstrated that ozonated oils could reduce inflammation and stimulate cell proliferation and tissue regeneration by increasing the supply of oxygen to ischemic or inflamed tissues (Kim et al. 2009, Silva et al. 2021, Xiao et al. 2017, Zanardi et al. 2008). The mechanisms, biological activity, and risks associated with ozonated oil have been described in detail elsewhere (Elisabetta et al. 2018, Leon et al. 2022).

Generally, the quality of ozonated oil is influenced by multiple operating parameters, including ozone concentration or purity, gas flow rate, types of vegetable oils, ozonation conditions (such as treatment time and acidity of the mixture), and the presence of other compounds like antioxidants or protic solvents. Optimizing these parameters is critical in achieving the desired lipid modifications. One common way to monitor and control the ozonation process is by measuring the peroxide value owing to its simplicity and speed. Apart from that, the quality of the ozonated samples can be assessed by analyzing various physicochemical properties such as acidity value, IV, viscosity, and melting and crystallization profiles (**Table 2**).

Ozone concentration is positively correlated with the ozonation rate. The use of concentrated or pure oxygen enhances the ozonation reaction, which in turn reduces the treatment duration (Díaz et al. 2012, Guerra-Blanco et al. 2021). The quality of the final products can also be influenced by the specific types of oils subjected to ozonolysis. An earlier investigation indicated that vegetable oils with a high degree of unsaturation, particularly rich in both linoleic and linolenic acids, tend to produce higher peroxide species or ozonide compounds with potent antimicrobial properties. For example, Díaz and colleagues (2006) reported that ozonated sunflower oil exhibited superior antimicrobial activity against *Pseudomonas aeruginosa* compared to ozonated olive oil. However, some studies demonstrated contradictory results. A study by Díaz et al. (2021) indicated that dendê oil showed a higher peroxide value (∼1.5-fold higher) compared to soybean oil, corn oil, and sunflower oil when the same ozone dosage was applied. The authors postulated that the chemical composition of dendê oil (high oleic acid) facilitates the reaction with ozone owing to its spatial conformation. Additionally, the study also reported that ozonated dendê oil exhibited high antimicrobial activity (Díaz et al. 2021). Previous studies have also indicated that the addition of antioxidants like ascorbic acid or decreasing the pH of oil may improve the stability of ozonated oil by either slowing down the degradation of ozonides or enhancing the stability of active peroxide species. This phenomenon can be attributed to the enhanced stability of ozone and its faster reactivity toward the C=C double bonds in fatty acids in an acidic environment (Enjarlis et al. 2022). Moreover, the presence of protic solvents, such as water or ethanol, can alter the final products in ozonated samples (Díaz et al. 2005, Moureu et al. 2015, Omonov et al. 2011). **Figure 1** demonstrates that the presence of water resulted in a shift in the formation of hydroxyl-hydroperoxides. Although there have been studies on ozonated oil, there is still a lack of comprehensive information on how various operating parameters collectively affect its quality. Therefore, further investigation and improvement are needed to advance our understanding in this area.

Recently, ozonated oil has been utilized in the food industry to prolong the shelf life of food products. For example, ozonated extra virgin olive oil was incorporated at a 2% concentration in the preparation of beef hamburgers to increase their shelf life. The outcome of this experiment revealed that the ozonated oil acted as a potent biologically active and antimicrobial agent, which significantly reduced the total viable count of lactic acid bacteria, Enterobacteriaceae, and coliforms present in the hamburgers (Ebrahimi et al. 2022). Another study illustrated the potential application of ozonated sunflower oil at varying peroxide concentrations as an effective antibacterial agent against *Escherichia coli* in goat, cow, and sheep milk (Guadalupe Armas et al. 2022). These results are an open door to new applications of ozonated oils.

3.5. Ultrasound

Ultrasound is a nonthermal processing method that typically uses a sound frequency higher than 20 kHz. It can be used to modify the physicochemical properties of lipids, such as crystallization, melting, and emulsification behavior. The mechanism comes from acoustic cavitation, i.e., the formation and sudden collapse of tiny gas bubbles, created by ultrasound in aqueous systems, which leads to material modification, creating a difference in temperature, pressure, and shear forces in the microenvironment that facilitates the mixing of the lipid components and causes several physicochemical changes in new lipid structures (Bansode & Rathod 2017).

Table 2 Key parameters and their corresponding results for ozonation

Operation parameters	Results	Reference
■ Oil sample: rice bran oil ■ Ozone concentration: 440 mg/L ■ Ozonation time: 246 min ■ Other operating condition: pH 4 (addition of ascorbic acid solution) ■ Presence of water ■ Gas flow rate: 0.1075 mg/mL/h	■ PV: 5–55 mEq/kg ■ AV: 1.3–2.3 mg NaOH/g ■ IV: 3.2–147 g I_2/100 g ■ Viscosity: 0.034–0.042 cp ■ Density: 0.83–0.918 g/cm^3	Enjarlis et al. 2022
■ Oil sample: olive oil ■ Ozone dose: 5 g O_3/g oil ■ Ozonation time: 100 min ■ Gas flow rate: 0.5 L/min	■ PV: 0.9–922.6 mEq/kg ■ AV: 1.12–1.36 mg KOH/g ■ IV: 73.4–80.2 g I_2/100 g ■ Oleic acid and linoleic acid reduced by 29% and 44% to 51.24% and 6.44%, respectively ■ Increase in aldehyde content (hexanal and nonanal) ■ Density: 0.917–0.965 g/cm^3 ■ Antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, *Candida albicans*, *Aspergillus brasiliensis*	Radzimierska-Kaźmierczak et al. 2021
■ Oil sample: neem oil ■ Ozonation time: 12 h ■ Gas flow rate: 63 mg/min ■ Other operating condition: absence and presence of water (10%)	■ AV: 6.5–39.8 and 117.4 mg KOH/g ■ IV: 0–69.1 for both systems at a rate of 8.6% IV reduction/h and 16% IV reduction/h ■ Higher crystallization onset temperature (due to higher peroxide compounds and depletion of unsaturated compounds with the increase in the ozonolysis reaction time) ■ Melting point shifted to higher values because of the saturation of fatty acid double bonds	de Oliveira et al. 2017
■ Oil sample: sesame oil ■ Ozonation time: 120 min ■ Ozone concentration: 45 mg/L ■ Gas flow rate: 1.5 L/min	■ PV: 198–4,542 mEq/kg ■ IV: 25.1–113.7 g I_2/100 g ■ Viscosity: 59.9–984 mPa·s	Sega et al. 2010
■ Oil sample: coconut oil ■ Ozone concentration: 37.5 mg/L ■ Ozonation time: 74.4 min ■ Gas flow rate: 54 L/h ■ Other operating condition: absence and presence of water (10%) or ethanol (10%)	■ PV: 263.7, 325.2, 463.2 mEq/kg ■ AV: 5.26, 6.01, 7.05 mg KOH/g ■ Viscosity: 57.3, 62.7, 66.5 mPa·s ■ Antimicrobial activity against *Pseudomonas aeruginosa* and *S. aureus*	Díaz et al. 2005
■ Oil sample: SO, flaxseed, and baru almond oils ■ Ozone concentration: 60 μg/mL ■ Ozonation time: 24 h (flaxseed oil) and 36 h (sunflower and baru almond oil) ■ Gas flow rate: 1 L/min ■ Other operating condition: presence of water (9%)	■ PV (SO: 20–2,152 mEq/kg; baru almond oil: 16–1,989 mEq/kg; flaxseed oil: 45–2,017 mEq/kg) ■ AV (SO: 0.2–10.7 mg KOH/g; baru almond oil: 0.3–8.0 mg KOH/g; flaxseed oil: 0.9–4.3 mg KOH/g) ■ IV (SO: 0.5–114.1; baru almond oil: 0.7–89.5; flaxseed oil: 444.6–175.1 g I_2/100 g) ■ Higher crystallization onset temperature with increasing ozonation time ■ Melting point shifted to higher values with increasing ozonation time ■ Antimicrobial activity against *E. coli* and *S. aureus*	de Almeida Kogawa et al. 2015

(*Continued*)

Table 2 ***(Continued)***

Operation parameters	Results	Reference
■ Oil sample: HOSO and SO ■ Ozone concentration: 65 mg/L ■ Ozonation time: 1–7 h ■ Gas flow rate: 30 L/h ■ Other operating condition: absence and presence of water (10%)	■ PV: 2,680 mEq/kg and 1,950 mEq/kg for HOSO and SO, respectively (presence of water) ■ PV: 400 mEq/kg for both HOSO and SO (absence of water) ■ AV: 31 and 32 mg KOH/g for HOSO and SO (presence of water), respectively ■ AV: 8 and 25 mg KOH/g for SO and HOSO (absence of water), respectively ■ IV not affected by the presence of water; HOSO reduced at a rate of 18 and 22 for HOSO and SO	Moureu et al. 2015

Abbreviations: AV, acid value; cP, g/100 s cm; HOSO, high oleic sunflower oil; IV, iodine value; PV, peroxide value; SO, sunflower oil.

One of the important processes in lipid modification is crystallization, as it influences the texture and sensory attributes of the final products, especially structural lipids such as margarine, cocoa butter, and spreads. Compared to conventional heating and cooling approaches, ultrasound has the advantage of controlling the size and distribution of crystals. Ultrasound-induced cavitation leads to the fragmentation or rupture of larger crystals, resulting in the formation of smaller crystals. Additionally, the intense energy released during cavitation promotes the redistribution of these crystals throughout the system, leading to a more uniform distribution (Chandrapala & Leong 2015). Ultrasound induces primary nucleation in nominally particle-free solutions at much lower supersaturation levels compared to conventional mechanical agitation-based crystallization. This may even eliminate the need for crystal seeding (Deora et al. 2013). A summary of the underlying mechanisms and influence of process variables of crystallization by ultrasound has been reviewed by Luque de Castro & Priego-Capote (2007). In a study by da Silva et al. (2021), high-intensity ultrasound (HIU) (20 kHz, 5 s, 0.3–0.7 kW/cm^2 was used to induce crystallization of mango kernel fat. The results showed that with ultrasound the onset of crystallization was earlier compared to without ultrasound. Additionally, the crystal size was smaller with the highest number of crystals and subsequently led to a sharper melting point of the fat (da Silva et al. 2021). Another work done by Sonwai and others (2021) shows the same trend when ultrasound (20 kHz, 10 s, 50% amplitude, 57 W) was applied to batch crystallization of palm-based fat. The size of fat crystals is smaller and comparable to scraped surface heat exchanger (SSHE) crystallization. The synergetic effect on reducing the fat crystal size was not obvious when both procedures (SSHE and HIU) were applied (Sonwai et al. 2021). Many other studies have also shown that ultrasound promotes small, uniform fat crystal size and increases the number of fat crystals such as in emulsion, oleogel, interesterified soybean oil, and organogels (da Silva et al. 2019, 2020; da Silva & Martini 2019; Jiang et al. 2019; Sharifi et al. 2019). The proposed mechanism of how ultrasound can help in crystallization is the induction of nucleation at lower saturation levels. Additionally, pulse (ultrasound) generates high shear that could disrupt crystal growth or promote big crystal breakdown and, subsequently, generate smaller crystals (Martini 2013, Maruyama et al. 2016). There is also an additional benefit in that it helps to prevent encrustation of crystals on the cooling elements, which ensures efficient heat transfer throughout the cooling processes.

The size, shape, and number of fat crystals are particularly important. They have a direct influence on the texture and sensory attributes of the final products. Utilizing ultrasound could improve the texture of the final products, as it could reduce the size of the fat crystal and enable significant reductions in processing times and the generation of higher-quality crystals. Fats with small crystal sizes (usually β′) have a smoother texture and creamier mouth feel compared to bigger sizes (Pande et al. 2013). Therefore, one could utilize ultrasound to improve texture, especially in structured fats such as margarine and shortening. Apart from enhancing textural attributes, the increase in the number of small fat crystals induced by ultrasound can also improve the oil binding capacity, as a strong network could be created and hold more liquid oils by the crystal network; the improvement is around 10 to 20% (da Silva & Danthine 2021, Giacomozzi et al. 2020, Li et al. 2021). This benefit allows the production of margarine, shortening, oleogels, or even spreads that utilize lesser amounts of saturated fat (usually the one that formed the crystal) while having higher amounts of unsaturated fats (the oil held by the crystal), meaning a healthier (as generally we assume unsaturated fats are healthier) product could be produced.

Although ultrasound appears promising in promoting fat crystallization, in practice, it is seldom employed in the industry. Many studies (mentioned above) are just batch crystallization conducted at lab scale using a single probe ultrasound source. For a large scale, a multiprobe must be installed and the effect of the multiprobe should be studied. However, this may be impractical, as the cost and the efficiency might not be as good as at lab scale. The localization of ultrasound may induce heat at large scales, and the heat transfer is different from that at small scales. Heat generated at large scales might be high and the increase in temperature might influence the crystallization process. In da Silva & Martini's (2019) work, it was reported that continuous application of HIU with 20 kHz and 108 W did not improve crystal size, shape, and oil binding capacity compared to lower watt and pulse application. This might be due to the continuous application of high-watt ultrasound causing higher shear forces and pressures, inducing extra heat and causing the temperature to rise. For those who are interested in using ultrasound for the crystallization process, it is essential to take note of the ultrasound power and duration used. Another potential drawback of ultrasound is that it might cause lipid oxidation owing to the generation of reactive oxygen species (Li et al. 2021). An in-depth study should be conducted to evaluate the side effects that can deteriorate oil quality.

Today's industrial practices often involve the use of an SSHE to produce structured fats. The use of ultrasound coupled with an SSHE seems to improve the quality of the product. But some studies have shown that without ultrasound, an SSHE alone is enough to produce a good quality product. A fair comparison of an SSHE with/without ultrasound should be conducted. One should optimize the product condition of SSHE first before they use an ultrasound-facilitated process. Nevertheless, ultrasound can be still considered as a potential tool to improve product quality.

4. CONCLUSIONS AND FUTURE OUTLOOK

Nonconventional technologies have demonstrated potential in revolutionizing lipid modifications across various applications. In this review, we have explored the applications of nonconventional technologies, including HPP, PEFs, ultrasound, ozonation, and CP technology, in lipid modifications. These nonconventional technologies offer several advantages over traditional methods, with increased efficiency being one of the key benefits. For example, HPP has the potential to reduce energy consumption. Furthermore, these innovative technologies offer improved specificity, as exemplified by CP hydrogenation, which allows the production of saturated fat with minimal *trans*-fat formation. Additionally, these technologies contribute to enhanced sustainability, as they primarily employ physical approaches. They have been successfully employed in diverse sectors such as food science, pharmaceuticals, and bioenergy, enabling the development of innovative lipid-based products with enhanced functionalities. For instance, HPP and ultrasound can improve crystallization, whereas CP technology can be employed in hydrogenation. Additionally, ozonation has the potential to extend the shelf life of food products by promoting the production of ozonides and peroxide species. As the methods have similar beneficial effects, coupling of these nonconventional technologies could be explored to see potential synergistic effects. Given that HPP and ultrasound are both related to crystallization, whereas CP and PEF are related to ionization, conducting studies on their coupling could lead to valuable improvements and benefits. The integration of these emerging green technologies with conventional methods (interesterification, hydrolysis or esterification, and fractionation) represents a relatively unexplored and inadequately studied research area. This interdisciplinary approach may have the potential to modify the functionality and physical properties of lipids. For instance, the concurrent utilization of CP technology along with interesterification, hydrolysis, or esterification could potentially tailor lipid structures with desirable characteristics and provide improved efficiency and ease of manufacturing.

However, despite the promising published data seen above, in most cases, there is no decisive success in the food industry. Although nonconventional technologies offer numerous advantages, several challenges need to be addressed. Studies are needed to examine the complex mechanisms involved in fat/oil crystallization, and the parameters governing scale-up need focus. Future research should report standardized process parameters to facilitate comparisons between studies. Numerical modeling such as computational fluid dynamics coupled with population balance modeling can provide some insight into and better understanding of some of the phenomena involved. Additionally, nonconventional technologies may give rise to unintended effects or by-products such as lipid oxidation, the creation of *trans*-fatty acids, or polymerization. Therefore, a thorough study should be conducted to minimize or prevent unintended by-product production, as these by-products might have negative side effects on the human body if they are consumed by or applied to humans.

In conclusion, the application of nonconventional technologies can provide several benefits by altering the molecular structures and the physicochemical behaviors of fats and oils, but it also comes with its own set of challenges. Some of the key challenges include:

1. Initial investment: Many industries may hesitate to adopt these technologies because of significant upfront costs.
2. Lack of expertise: These technologies are relatively new and may require specialized knowledge and expertise for proper implementation.
3. Integration with existing systems: Ensuring compatibility and smooth integration with other systems in place may pose challenges.
4. Regulatory hurdles: In some cases, the lack of well-defined regulations or standards can lead to uncertainties in obtaining permits or approvals.
5. Scalability: Some of the nonconventional technologies may work well in small-scale operations but face challenges when applied in large-scale industrial operations.
6. Reliability and robustness: Nonconventional technologies might still be at the developmental stage, making them less proven and, potentially, less reliable.
7. Product quality: Safety, stability, and potential unwanted by-products that might be produced from nonconventional technologies should be further studied and mitigated.

Despite these challenges, with continued research, development, and support from the industry and regulatory bodies, nonconventional technologies have the potential to drive innovation in the field and contribute to sustainable and efficient practices.

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The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

AUTHOR CONTRIBUTIONS

Phuah Eng-Tong, Lee Yee-Ying, Tang Teck-Kim, and Lai Oi-Ming worked on the conceptualization of the review, wrote the original draft, and reviewed and edited the article prior to submission. Casimir Akoh, Cheong Ling-Zhi, Tan Chin-Ping, and Wang Yong reviewed and edited the article prior to submission.

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