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Microfluidic Chips in Food Science: From Principles to Applications and Beyond

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Abstract

The microfluidic has emerged as a promising platform to manipulate the fluid in micro scale. It has been widely used in multiple fields, *e.g*., biomedical engineering, analytical chemistry, environment detection, and drug screening. Recently, the application of microfluidic chip has been extended to the food science. The microfluidic chip can be used to fabricate food delivery systems, *e.g*., emulsions, lipid vesicles, microparticles, and microcapsules. These systems encapsulate the bioactive substances that are highly nutritious but sensitive to environmental factors. Another application of microfluidic chip in food science is to detect food hazards. It has exhibited several advantages, such as portability, ease to manipulate, low cost, and low sample consumption. Moreover, the nutrition delivery systems show excellent performances in monodispersity, size uniformity, and also stability. The microfluidic chip for food science has attracted considerable attention and is still developing rapidly. To make this novel technique well-known to the researchers in this field, we summarized the advances of microfluidic technology in food science, including the design of microfluidic chips, and the detailed applications. At the end, we proposed the current challenges and possible solutions, and prospected the future development.

1. Introduction

Microfluidic is a novel platform which enables the precise control of fluids at the micro- and nanoscale. As an emerging interdisciplinary technology, microfluidic involves physics, chemistry, biology, and material science. Due to its excellent ability to manipulate fluid interfaces at the micro- and nanoscale, microfluidic has become a promising tool for the design, preparation of novel functional materials with controllable microstructures. Nowadays, microfluidic has found widespreading applications in various fields, such as biomeidical engineering, analytical chemistry, environment detection, and drug development.

In the field of food science, microfluidic has also attracted considerable attention as it shows superiority in fabricating food delivery systems such as emulsions, lipid vesicles, microparticles, and microcapsules[(Visser et al. 2018)]. These delivery systems hold significant value for encapsulating, transporting, protecting, and controlling the release of beneficial substances like nutrients, active ingredients, and flavor compounds[(Ganesan et al. 2018)]. In the traditional methods, these delivery systems are fabricated by the mechanical stirring, high-pressure homogenization, fluid shearing, and interfacial polymerization. These methods rely on equipment such as high-pressure homogenizers, ultrasonic homogenizers, stirrers, colloid mills, and disc dispersers. However, these methods often face challenges in controlling particle size distribution and optimizing structural designs[(Celli et al. 2015; Maan et al. 2011)]. In comparison, food delivery systems developed through microfluidic technology offer superior monodispersity, size uniformity, and also stability[(Liu et al. 2017)].

Additionally, microfluidic is widely used in the detection and analysis of food hazards such as foodborne pathogens, pesticide residues, and heavy metals. It is considered as a promising tool in these areas due to the following advantages, minimal sample usage, high detection efficiency, and ease of

operation[(Noviana et al. 2020)]. Traditional methods for detecting food hazards include chromatography, plate culture based biological identification, and enzyme-linked immunosorbent assays (ELISA). However, these methods often require long sample processing times and high costs. In contrast, microfluidic technology integrates multiple laboratory operation, such as sampling, dilution, reagent addition, reaction, separation, and detection, into a single device. Moreover, this technique can reduce reagent consumption, speed up screening processes, shorten reaction times, and lower detection costs. Therefore, it has significantly improved the efficiency and portability of detection equipment.

Although microfluidic has been used in food science, some researchers in this field are still unfamiliar with this novel technique. Therefore, we have reviewed the microfluidic for food science in this paper. This paper provides an overview of the history of microfluidic, fluid flow states in microfluidic, droplet formation methods, types of microfluidic chips, and the applications in food science. Special interests are focused on the preparation of food delivery systems, *e.g*., emulsions, lipid vesicles, microparticles, and microcapsules, and also the detection of food hazards. At the end, we conclude this paper by discussing the future prospects of microfluidic technology in the food science.

2. History of microfluidic technology

The concept of "microfluidics" can be traced back to the 1970s, when researchers fabricated gas chromatographs on silicon wafers using photolithography. Subsequently, microfluidic capillary electrophoresis devices and microreactors emerged. In 1990, Manz and Widmer proposed the term “microfluidic chip” for the first time. In 1992, Bloomstein et al.[(Bloomstein and Ehrlich 1992)] used laser etching to fabricate a three-dimensional microfluidic device by assembling silicon components. In 1995, Mathies et al. [(Woolley and Mathies 1995)] implemented the ultra-fast DNA sequencing on a micro-capillary electrophoresis chip, sequencing approximately 150 basic group in 540 seconds with 97% accuracy. In 1996, Woolley et al.[(Woolley et al. 1996)] integrated polymerase chain reaction (PCR) with capillary electrophoresis on a microfluidic chip, enabling multi-channel DNA sequencing on a microfluidic platform. In 1998, Chiem et al.[(Chiem and Harrison 1998)] used microfluidic chips to measure the affinity constant of a monoclonal antibody for a fluorescent-labeled bovine serum protein in mouse ascites fluid through affinity capillary electrophoresis experiments.

In 2000, Umbanhowar et al.(Umbanhowar et al. 2000) developed the method to fabricate the highly monodisperse emulsions using microfluidic technology. They produced emulsions with droplet sizes ranging from 2 μm to 200 μm and low polydispersity(as low as 3%). In the same year, Sugiura et al.[(Sugiura et al. 2000)] combined photolithography with etching techniques to fabricate a silicon-based microfluidic chip, which was successfully used to produce lipid vesicles with an average particle size of 21.3 μm and a coefficient of variation of 4.1%. In the early 21st century, polymer materials were introduced into the fabrication of microfluidic chip. In 2004, Seo et al. [(Seo and Lee 2004)] developed a microfluidic chip integrated with the self-aligned planar micro-lens using polydimethylsiloxane (PDMS). This device improved the sensitivity, reduced the focusing time, and therefore was positioned as a low-cost, fast, and

highly sensitive diagnostic tool. In 2005, Lorenceau et al.(Lorenceau et al. 2005) used double emulsions as templates for the precise assembly of polymer vesicles. In 2006, Whitesides et al. (Gao et al. 2020) proposed the concept of paper-based microfluidic chips. These chips were low-cost, simple to fabricate, highly sensitive, easy to use and transport, and required minimal sample volumes, offered fast analysis speed. These advantages highlighted their potential for food safety testing applications. In 2008, Shum et al. (Shum et al. 2008) employed double emulsions as templates to create lipid vesicles with high encapsulation efficiency. In 2010, Shum et al.(Shum et al. 2010) further demonstrated the controlled preparation of monodisperse, non-spherical particles using microfluidic chips.

Over the past few decades, the applications of microfluidic technology have expanded rapidly across multiple fields (Fig. 1). It has provided a new, efficient method for preparing monodisperse droplet structures.(Ge et al. 2016). The ability of microfluidic chips to precisely manipulate fluids under mild processing conditions allows for the production of uniform simple droplets and the complex multi-droplet structures with promising applications(Chen et al.).

3. Fluid Flow States in Microfluidic Chips

Microfluidic technology controls fluid flow by confining it within designed microchannels, minimizing the influence of environment and enabling precise regulation of fluid flow. The state of fluid flow can be qualitatively described with dimensionless physical parameters, such as the Reynolds number (Re), Weber number (We), and Capillary number (Ca), which are key parameters for characterizing fluid flow in microfluidic chips(Celli and Abbaspourrad 2018).

The forces that affect fluid flow includes two types, the body forces, *e.g*., gravity force and inertial force, and the surface forces, *e.g*., the surface tension forces. However, in microscale, the fluid flow is dominated by the surface forces, and the body forces become insignificant. The We, a dimensionless parameter that compares inertial forces to surface tension, is used to determine the relative importance of inertial effects(Baroud and Willaime 2004). Usually the We is small for the microscale fluid flow. Fluid flow is generally categorized into two types, the laminar flow and turbulent flow, which can be determined by the Re, the ratio of inertial forces to viscous forces. When Re < 2300, the fluid takes laminar flow, when Re is large, the flow becomes turbulent. In microfluidic chips, the Re is typically below 100, indicating that the fluid flow is in the laminar regime (Chen et al. 2021; Feng and Lee 2019).

In food science, microfluidic technology is mainly used to fabricate delivery systems such as emulsions, lipid vesicles, microparticles, and microcapsules, where droplets serve as fundamental structural units. The flow state of the fluid plays a crucial role in determining the formation of droplets within the microchannel. In the next section, we will discuss the droplet formation mechanisms in detail.

3.1 Modes of droplet formation

The Ca, the ratio of viscous forces to surface tension, is frequently used to qualitatively characterize the mode of droplet formation. When Ca < 0.01, droplets form through a squeezing mechanism. If 0.01 < Ca < 0.3, droplets form by dripping. For an even higher Ca values, droplets form via jetting[(Geng et al. 2020)]. The dynamic breakup and coalescence of interfaces between immiscible fluids results in the droplet formation. The length of the microchannel is much larger than its width, resulting in a small cross-sectional area. In this circumstance, the body forces, including the inertial force and gravity force can be neglected, making viscous shear forces and surface tension force dominant the droplet formation. During this process, the droplet blocks the channel and experiences the hydrostatic pressure from the surrounding fluid. Thus, droplet formation is affected by the interplay of three key factors: the viscous shear force exerted by the continuous phase on the dispersed phase, the surface tension force resisting droplet detachment, and the pressure acting on the droplet when it obstructs the microchannel.

Viscous shear force depends on both the viscosity and flow rate of the fluids. By varying the viscosity ratio and the flow rate ratio between the continuous and dispersed phases, it is possible to modulate the magnitude of the shear force. The surface tension force plays an essential role in determining droplet size by hindering the detachment of the droplet. Since surface tension force is a function of the materials, adding surfactants can reduce this force, thereby facilitating droplet detachment. Two simultaneous processes, *i.e*., the droplet expansion and surfactant adsorption at the interface, take place during droplet formation. Both of these two processes can influence the effective surface tension force. When droplet expansion occurs faster than surfactant adsorption, the surface tension becomes more influential. Conversely, if surfactants adsorb more rapidly than the droplet expands, surface tension plays a lesser role. In practice, droplets tend to expand rapidly, making it difficult to accurately predict their size or the exact value of the surface tension force [(Maan et al. 2015)].

As shown in Fig. 2, the droplet formation mechanism can be divided into three modes, squeezing, dripping and jetting, depending on the position at which the droplet forms and the process of formation [(Muijlwijk et al. 2016)]. In the following, we would discuss these three modes in detail.

In the squeezing mode, the viscous shear force exerted by the continuous phase is insufficient to detach the droplet rapidly from the tip of the dispersed phase. As the dispersed phase continues to flow into the microchannel, the droplet at its tip expands, gradually blocking the flow of the continuous phase. The growing droplet experiences pressing force at the neck from the continuous phase, ultimately leading to its detachment and dispersion into the continuous phase. In this regime, the droplet formation frequency is relatively low, and the size of the droplet is independent of fluid viscosity and surface tension. Instead, droplet size is primarily affected by the flow rate ratio between the continuous and dispersed phases. The dominant force in the squeezing mode is pressing force. The droplet size increases as the flow rate ratio increases, and the viscosity ratio between the fluids has minimal influence.

In the dripping mode, the viscous shear force from the continuous phase is sufficient to detach the droplet from the dispersed phase before it blocks the microchannel and the flow of continuous phase. In this regime, droplet formation depends on the balance between viscous shear force and surface tension.

When the droplet reaches a critical size, this balance is disrupted, and the shear force exceeds the surface tension, causing the droplet to detach. The dripping mode leads to a higher frequency of droplet formation than the squeezing mode, producing droplets with a more uniform size distribution. The size of the droplets is mainly influenced by the viscous shear force. The influence of flow rate ratio on the droplet size becomes weaker than it in the squeezing mode. Increasing the viscosity ratio between the fluids in this regime can result in smaller droplets.

In the jetting mode, the fluid flow rates increase substantially, leading to a continuous rise in the shear force. As a result, the location of droplet formation shifts downstream along the microchannel. However, the droplet size distribution becomes broader. The onset of jetting is associated with Rayleigh-Taylor instability, and the system approaches a critical state where the continuous and dispersed phases may flow in parallel without forming discrete droplets[(Opalski et al. 2019; Shang et al. 2017; Utada et al. 2007)]. In the jetting mode, increasing the flow rate can cause a decrease in droplet size. For stable droplet formation, the viscosity of the continuous phase should be several times or even tens of times greater than that of the dispersed phase. Otherwise, parallel flow of the two phases may occur, without forming discrete droplets[(Muijlwijk et al. 2016)].

4. Types of microfluidic chips

Microfluidic chips are fabricated from various materials, including inorganic materials such as quartz, glass, metals, and silicon, as well as organic polymers like polymethyl methacrylate (PMMA), polycarbonate (PC), polydimethylsiloxane (PDMS), and epoxy resins. Among these, PDMS is the most widely used material due to its excellent optical transparency, chemical inertness, low cost, non-toxicity, and ease of fabrication. Microfluidic chips designed for droplet generation can be classified into three-dimensional microfluidic chips with glass capillaries and planar microfluidic chips made from elastic polymers like PDMS. Additionally, paper-based microfluidic chips are widely used in food safety testing due to their biodegradability, low cost, broad applicability, and compatibility with various chemical substances. In the following, we would discuss these microfluidic chips in detail.

4.1 Three-dimensional microfluidic chips with glass capillaries

Microfluidic chips with glass capillaries typically are composed of two coaxial glass capillaries with different sizes. These chips are fabricated by inserting one or two cylindrical glass capillaries into a square glass capillary. The cylindrical capillaries have tapered tips, and their outer diameters are slightly smaller than the inner size of the square capillary to ensure coaxial alignment[(Shang et al. 2017)], as shown in Fig. 3. These glass-based microfluidic chips can be categorized into co-flow, cross-flow, and hybrid co-flow/cross-flow configurations. For the co-flow configuration, the dispersed phase flows inside the inner cylindrical capillary, while the continuous phase flows through the space between the inner and outer capillaries. The continuous phase envelops the dispersed phase, and the interaction at the tip of the

inner capillary leads to droplet formation through the shear forces exerted by the continuous phase. In contrast, cross-flow microfluidic chips are different which the dispersed phase enters from one end of the outer capillary, while the continuous phase flows from the other end, where droplet formation occurs (Celli and Abbaspourrad 2018; Ushikubo et al. 2015). This type of microfluidic chips is widely used in laboratory to fabricate discrete droplets since its advantages in chemical resistance, efficient heat transfer, ease of localized surface modification within the microchannels, and precise control over droplet structures (Shah et al. 2008; Zhao et al. 2017).

4.2 Planar microfluidic chips with elastic polymers

Planar microfluidic chips, typically fabricated from materials like PDMS, offer flexibility in both materials and fabrication methods, with various chip designs for different applications. The microchannels in these chips are generally rectangular in the cross-section. Planar microfluidic chips can be categorized into four primary types based on their geometry, T-junction design, Y-junction design, cross-junction and double cross structure design, as illustrated in Fig. 4.

In the planar microfluidic chips with T-junction, the continuous phase and the dispersed phase flow through two orthogonal microchannels. Droplets formation usually occur via a pinching mechanism, where the dispersed phase is squeezed at the junction by the continuous phase. This type of microfluidic chips are widely employed in producing monodisperse droplets. In the Y-junction microfluidic chips, droplets are generated in one step, and the droplet size is highly sensitive to the operational conditions(Feng and Lee 2019). In the microfluidic chips with cross-junction and double cross-junction, the microchannels of the continuous and dispersed phases meet at a cross intersection. The intersecting flows restrict each other, offering excellent control over molecular diffusion between phases, which makes these chips well-suited for self-assembly processes. Compared to T-junction and Y-junction chips, cross-junction microfluidic chip leads to a strong shear forces at the intersection, facilitating the generation of smaller droplets. However, controlling the uniformity of droplet sizes, *i.e*., monodispersity, becomes more challenging in this configuration (He et al. 2020; Liu et al. 2017).

4.3 Paper-based microfluidic chips

Paper-based microfluidic chips are emerging in recent years, and have been widely used in the field of food detection and analysis. The chips can be integrated with other technologies, such as surface enhanced Raman spectroscopy detection, colorimetric detection, and electrochemical analysis(Ray et al. 2022). For the detection of different substances, filter paper or other paper materials are usually selected as the base material. Filter paper is one of the most commonly used base materials due to its strong hygroscopicity. Pure fiber porous membranes such as graphite paper and chromatography paper can also be used as base materials.

Usually, hydrophobic substance is combined with the base paper material. Commonly used hydrophobic substances include photoresist, PDMS, wax, polystyrene (PS), alkyl ketene dimer (AKD), etc. The

fabrication methods of paper-based microfluidic chips are divided into physical deposition method, physical barrier method and chemical modification method. Both of the physical deposition method and physical barrier method change the wettability of paper through the physical interaction between the hydrophobic substance and the paper. As to the chemical modification method, it generates a hydrophobic boundary by introducing hydrophobic groups on the cellulose molecular chain. According to the direction of fluid flow, it can be divided into two-dimensional paper microfluidic chips and three-dimensional paper microfluidic chips. The fabrication of two-dimensional paper-based microfluidic chips is relatively simple. For three-dimensional chips, they are fabricated by folding or stacking the papers. Compared with two-dimensional paper-based microfluidic chips, three-dimensional chips can make the fluid flow in the horizontal and vertical directions, and have the feasibility of implementing the simultaneous detection of multiple substances.

5. Applications of microfluidics in food science

With well-established fabrication strategies, microfluidic techniques and derived materials have found broad utility in fundamental research and industrial sectors ranging from biopharmaceuticals, biomaterials and medical devices to food science. Notably, microfluidic-synthesized materials possess favorable encapsulation and controlled-release performance, rendering them attractive candidates for food science and engineering. This section summarizes microfluidic products generated via diverse fabrication routes, including emulsions, lipid vesicles, microparticles and microcapsules, and systematically discusses their food-related applications (Fig. 5). Beyond these material-based applications, we address microfluidic platforms for food safety analysis, reinforcing the intrinsic link between microfluidics and food science.

5.1 Fabrication and application of emulsion

Emulsions are usually composed of two insoluble liquids mixture, with one liquid (as dispersed phase) dispersed in the form of droplets into the other liquid (as the continuous phase). They usually require the addition of surfactants to avoid the coalescence of dispersed phase. Most emulsions are transparent or translucent, and low viscous. The most common emulsions are oil-in-water (O/W) and water-in-oil (W/O) systems. There are also multiple emulsions with more complex structures, such as water-in-oil-in-water (W/O/W) and oil-in-water-in-oil (O/W/O) systems[(Espitia et al. 2019)]. Emulsions have the advantages of small particle size and high transparency, and are often used as a food delivery system with excellent performance. They can not only serve as carriers for delivering substances, but also increase the solubility of nutritional functional ingredients, pigments. Emulsions have shown great potential applications in the food science, and have therefore attracted considerable attention.

Microfluidic technology has the advantages of low energy consumption, milder processing conditions, and strong controllability. The droplets often have good monodispersity and low coefficient of variation[(Muijlwijk et al. 2016)]. Another advantage of microfluidic technology is that it can precisely control

the fluid flow and the formation of droplet structures at the microscale, which makes it a promising method in the fabrication of food delivery systems.

For foods encapsulation, Gao et al. (Gao and Chen 2019) designed a microfluidic chip to prepare S/O/W and S/W/O double emulsion structures, and the encapsulation success rate was close to 100%. Comunian et al. (Comunian et al. 2017) used a microfluidic chip to fabricate O/W/O double emulsions encapsulating health-beneficial echium oil. Al Nuumani et al. (Al Nuumani et al. 2020) used a coaxial microfluidic chip to encapsulate concentrated sucrose solution in oil droplets stabilized by starch. They successfully generated a monodisperse W/O/W double emulsion composed of a starch-coated oil shell and a water core. They demonstrated the possibility of maintaining the sweetness of sucrose through the structural characteristics of the emulsion while reducing the sugar intake. Pessi et al. (Pessi et al. 2014) used glass capillary microfluidic chip to fabricate W/O/W double emulsion encapsulating bovine serum albumin (BSA), with an encapsulation rate of 84%. The emulsions prepared by microfluidic chip have shown good monodispersity, uniform size distribution, and good stability, providing more possibilities for the encapsulation in food science.

5.2 Fabrication and application of lipid vesicles

Lipid vesicles, typically composed of multiple phospholipid bilayers with biological membranes, usually have excellent water dispersibility. These vesicles encapsulate hydrophilic or lipophilic components, enhancing the bioavailability of active compounds while maintaining the structural stability. In food science, lipid vesicles are commonly used to encapsulate lipids, antioxidants, minerals, vitamins, proteins, and various enzymes. As an advanced technology, lipid vesicles provide solutions for controlled release of functional ingredients, improving bioavailability and extending shelf life. Encapsulating bioactive compounds which are unstable and prone to oxidation in external environments into lipid vesicles offers protection, ensuring their stability and increasing the storage time.

Traditional methods for lipid vesicles fabrication include ethanol injection, freeze-thaw cycles, thin-film ultrasound dispersion. However, these techniques are not satisfying because of their low vesicle concentration, large particle size, low encapsulation efficiency and high costs. Microfluidic technology can address the above issues by enhancing vesicle concentration in the dispersed phase, increasing the encapsulation efficiency of active compounds, and reducing production costs(Aranguren et al. 2020). Arriaga et al.(Arriaga et al. 2014) proposed a method for the continuous high-throughput production of ultrathin lipid vesicles to achieve precise control over vesicle size and lipid composition. Marze et al. (Marze et al. 2014) used the microfluidic chip to simulate the digestion of lipophilic vitamins in the gastrointestinal tract. Michelon et al. (Michelon et al. 2017) fabricated β-carotene-encapsulated lipid vesicles and then evaluated the encapsulation efficiency of β-carotene exceeded. Additionally, altering the microchannel geometry enabled precise control over vesicle size distribution, which is a crucial parameter that influences the residence time of lipid vesicles within the human body(Kennedy et al. 2012).

About size distribution studies, Michelon et al. [Michelon et al. 2019] fabricated the giant lipid vesicles with the size of 100 ~ 180 μm in diameter. They used the low-toxicity solvents such as ethyl acetate and pentane, combined with non-purified soybean lecithin, a cost-effective food-grade phospholipid blend. Through solvent evaporation and dehydration, they obtained the oil phase used for vesicle generation. The resulting vesicles exhibited uniform size and structural consistency, making them well-suited for practical applications. Microfluidic technology plays a critical role in enhancing lipid vesicle production by ensuring uniform size distribution and generating structures optimized for real-world use, paving the way for broader applications in food science.

5.3 Fabrication and application of microparticles

Microparticles are small particles with diameters ranging from a few micrometers to several hundred micrometers, including microspheres and microgels. These particles, formed by solidifying single or multiple emulsions, act as efficient carriers for encapsulating and delivering bioactive substances to specific targets. Microparticles can protect the compounds from the influence of environmental factors such as oxygen, light, and others. They can also enable the controllable release of the encapsulated substances in response to environmental triggers, such as temperature, pH, or enzymes[Feng and Lee 2019; Kim and Lee 2022; Ushikubo et al. 2015].

Traditional methods for microparticles fabrication include precipitation polymerization, emulsion polymerization, dispersion polymerization, SPG membrane emulsification, and layer-by-layer assembly. However, these methods are not satisfying with uniformity in size, shape, and composition, which limits their applications[Wang et al. 2017]. Microfluidic technology offers a platform to control the particle morphology and functional micro-particles with complex structures. Zhang et al. [Zhang et al. 2022] utilized 3D-printed microfluidic devices to fabricate vitamin A-encapsulated microgel particles. The two nature materials, sodium alginate and gelatin, are used as continuous-phase. This method improved the stability of vitamin A, ensuring it reached the intestines without degradation by stomach acid. Robinson et al. [Marengo et al. 2019] generated egg white/carrageenan droplets in an oil phase. By using glutaraldehyde-induced chemical crosslinking and microwave radiation induced physical crosslinking, the droplets were solidified into micro-particles which exhibited hydrophilic behavior in oil media and gradually released their contents in water over several months while maintaining stability.

Sensitive and complex structure microparticles were displayed. Chen et al. [Chen et al. 2017] employed glass capillary microfluidic chips to produce shellac solid particles encapsulating β-carotene. This study has expanded the application of β-carotene in food science. Hsiao et al. [Hsiao et al. 2020] using microparticles encapsulate chlorophyll, which can be used as a natural food pigment, with polycaprolactone(PCL). Tie et al. [Tie et al. 2021] developed a PDMS microfluidic chip to generate alginate/chitosan micro-particles for encapsulating proanthocyanidins using a W/W/O double emulsion template. These particles featured a core-shell structure and were fabricated through internal-external gelation. The particles showed pH-responsive release behavior in simulated gastrointestinal fluids.

5.4 Fabrication and application of microcapsules

Microcapsules are solid microparticles encapsulating solids, liquids, or gases within a tiny capsule. Their diameters typically range from a few micrometers to several millimeters. The external layer, referred to the wall material, is typically made of natural or synthetic polymers. For their morphology, microcapsules can be spherical, clustered, or irregular in shape. Based on the number of core materials, they can be classified into single-core or multi-core capsules. Based on the number of wall layers, they can be classified into single-layer, double-layer, or multi-layer capsules. The capsule walls serve as protective barriers, shielding core materials from adverse environmental conditions. The microcapsules facilitate the encapsulation, transport, controlled release, and protection of bioactive compounds(Datta et al. 2014).

The traditional methods to fabricate microcapsules include interfacial polymerization, complex coacervation, gel embedding, and spray drying. However, these methods often yield microcapsules with inconsistent sizes, wall thickness, and structural composition, limiting their applicability in certain scenarios (Amato et al. 2017). In comparison, microfluidic technology offers significant advantages in the fabrication of microcapsules, such as high monodispersity, uniform size distribution. The capsule's shell thickness and composition can be precisely controlled by tuning experimental parameters. Kim et al.(Kim et al. 2011) produced W/O/W biodegradable microcapsules with ultra-thin walls (tens of nanometers). These capsules are suitable for encapsulating and delivering food nutrients. Ravanfar et al. (Ravanfar et al. 2018) employed a glass capillary microfluidic system combined with freeze-drying technology to encapsulate fish oil within microcapsules. The capsules used whey protein microgel and beet pectin composites as wall materials. The cross-linkers, laccase and calcium chlorides, were added to enhance stability. These microcapsules exhibited superior physicochemical stability compared to those produced by traditional homogenization methods.

For storage, Comunian et al. (Comunian et al. 2014) utilized palm oil as the oil phase and encapsulated ascorbic acid via microfluidic techniques. After 30 days, the retention rate of ascorbic acid remain 97% in the microcapsules, demonstrating the effective protection. Zhang et al. (Zhang et al. 2017) prepared microcapsules with ultra-thin inert polymer walls. They encapsulated amylase as the core material. The W/O/W emulsion-based capsules retained 85% of the amylase's activity after 47 days at room temperature, showcasing their potential for enzyme stabilization.

5.5 Detection and analysis of hazardous substances in food

Microfluidics enable the precise manipulation of small fluid volumes in microchannels with sizes down to tens of micrometers. It has shown significant advantages in miniaturizing the analytical devices, reducing costs, and enabling highly efficient detection of contaminants in food. In recent years, some novel microfluidic devices have emerged, such as paper-based microfluidic chips. These chips are low-cost, portable, and suitable for colorimetric analysis.

Microfluidic chips have become a new platform for fast and efficient analysis, playing an essential role in food hazard detection such as foodborne pathogens, pesticide residues, and heavy metals [(Zhao et al. 2019)]. Trofimchuk et al. [(Trofimchuk et al. 2020)] used paper-based microfluidic chips combined with colorimetric methods to detect the residual norfloxacin in fish, chicken, beef, and pork. El-Sharoud et al. [(El–Sharoud et al. 2013)] developed a microfluidic platform integrating PCR for detecting Cronobacter sakazakii in synthetic media and recombinant milk. Azizi et al.[(Azizi et al. 2019)] utilized droplet microfluidics with loop-mediated isothermal amplification (LAMP) to create a high-throughput biosensor for the rapid detection of Salmonella typhimurium. Maryam et al.[(Taghizadeh–Behbahani et al. 2022)] developed a paper-based microfluidic chip integrated with a colorimetric sensor to efficiently detect antibiotic residues in milk and eggs. Novo et al. [(Novo et al. 2013)] combined PDMS microfluidics with chemiluminescence-based indirect competitive ELISA to detect ochratoxin A in wine and beer extracts.

6. Summary and perspectives

In food industry, microfluidic technology allows precise control over droplet structures and properties by adjusting microchannel shapes, operating conditions (such as the flow rate ratio) and the physical characteristics of fluids (such as viscosity and surface tension). This technology enables the synthesis of various functional food structures. Food delivery systems, including single and multiple emulsions, lipid vesicles, particles, and microcapsules, are particularly valuable for encapsulating bioactive substances that are highly nutritious but sensitive to environmental factors. These systems ensure protection, controlled release, and enhancement of bioactives. The food delivery systems fabricated through microfluidic technology exhibit uniform size distribution and excellent monodispersity while being capable of carrying both hydrophilic and hydrophobic compounds. In food analysis, microfluidic technology offers significant potential by miniaturizing the size, automating the detection process, reducing costs and sample consumption. Through careful design of microchannel size and geometry, multiple detection components can be integrated into a compact chip. Additionally, microfluidic chips can be developed with multiple channels to enable simultaneous detection of various reactions, demonstrating promise for more efficient food testing.

The application of microfluidic technology in the food science is an emerging trend. However, there are still certain limitations. For example, the production throughput of current microfluidic devices is still not satisfying. Although increasing throughput is possible by parallelizing multiple droplet-forming microchannels within integrated microfluidic systems[(He et al. 2019)], this approach has not yet reached the scale necessary for industrial production, limiting its broader use in the food industry. Furthermore, the fabrication of microfluidic devices demands high technical expertise, and the cost of raw materials remains relatively high. In food analysis, many microfluidic chips are disposable, which increases the costs. Another challenge lies in integrating microfluidic chips with advanced detection technologies and external automated analysis and display equipment. To achieve industrial-scale application, it is essential to further improve manufacturing technologies, develop food-grade ingredients compatible

with microfluidic processes. These advancements will pave the way for high-throughput production and broader applications in the food industry.

Declarations

Conflicts of Interest:

None.

Author Contribution

Y.D. wrote the main part of this paper. W.K. prepared all the figures and selected the references. Y.Y. wrote and revised the manuscript. Q.Y. put forward the logic frame of this review and help edit the manuscript.

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References

1. Al Nuumani R, Vladisavljevic GT, Kasprzak M, Wolf B (2020) In-vitro oral digestion of microfluidically produced monodispersed w/o/w food emulsions loaded with concentrated sucrose solution designed to enhance sweetness perception. Journal of Food Engineering 267 https://doi.org/DOI
2. Amato DV, Lee H, Werner JG, Weitz DA, Patton DL (2017) Functional microcapsules via thiol ene photopolymerization in droplet-based microfluidics. Acs Applied Materials & Interfaces 9 (4):3288–3293 https://doi.org/DOI
3. Aranguren A, Torres CE, Munoz-Camargo C, Osma JF, Cruz JC (2020) Synthesis of nanoscale liposomes via low-cost microfluidic systems. Micromachines 11 (12) https://doi.org/DOI
4. Arriaga LR, Datta SS, Kim SH, Amstad E, Kodger TE, Monroy F, Weitz DAJS (2014) Ultrathin shell double emulsion templated giant unilamellar lipid vesicles with controlled microdomain formation. 10 (5):950–956 https://doi.org/DOI

5. Azizi M, Zaferani M, Cheong SH, Abbaspourrad A (2019) Pathogenic bacteria detection using rna-based loop-mediated isothermal-amplification-assisted nucleic acid amplification via droplet microfluidics. Acs Sensors 4 (4):841–848 https://doi.org/DOI
6. Baroud CN, Willaime H (2004) Multiphase flows in microfluidics. CR Phys 5(5):547–555. https://doi.org/DOI
7. Bloomstein TM, Ehrlich DJ (1992) Laser-chemical 3-dimensional writing for microelectromechanics and application to standard-cell microfluidics. Journal of Vacuum Science & Technology B 10 (6):2671–2674 https://doi.org/DOI
8. Celli GB, Ghanem A, Brooks MS-L (2015) Bioactive encapsulated powders for functional foods—a review of methods and current limitations. Food and Bioprocess Technology 8 (9):1825–1837 https://doi.org/DOI
9. Celli GB, Abbaspourrad A (2018) Tailoring delivery system functionality using microfluidics. 9(1):481–501https://doi.org/DOI
10. Chen D, Zhao C-X, Lagoin C, Hai M, Arriaga LR, Koehler S, Abbaspourrad A, Weitz DA(2017) Dispersing hydrophobic natural colourant β-carotene in shellac particles for enhanced stability and tunable colour. 4 (12):170919 https://doi.org/DOI
11. Chen L, Yang C, Xiao Y, Yan X, Hu L, Eggersdorfer M, Chen D, Weitz DA, Ye F (2021) Millifluidics, microfluidics, and nanofluidics: Manipulating fluids at varying length scales. Materials Today Nano 16 https://doi.org/DOI
12. Chiem NH, Harrison DJ (1998) Monoclonal antibody binding affinity determined by microchip-based capillary electrophoresis. ELECTROPHORESIS 19 (16–17):3040–3044 https://doi.org/DOI
13. Comunian TA, Abbaspourrad A, Favaro-Trindade CS, Weitz DA (2014) Fabrication of solid lipid microcapsules containing ascorbic acid using a microfluidic technique. Food Chemistry 152:271–275 https://doi.org/DOI
14. Comunian TA, Ravanfar R, de Castro MA, Dando R, Favaro-Trindade CS, Abbaspourrad A (2017) Improving oxidative stability of echium oil emulsions fabricated by microfluidics: Effect of ionic gelation and phenolic compounds. Food Chemistry 233:125–134 https://doi.org/DOI
15. Datta SS, Abbaspourrad A, Amstad E, Fan J, Kim S-H, Romanowsky M, Shum HC, Sun B, Utada AS, Windbergs M, Zhou S, Weitz DA (2014) 25th anniversary article: Double emulsion templated solid microcapsules: Mechanics and controlled release. Advanced Materials 26 (14):2205–2218 https://doi.org/DOI
16. El-Sharoud WM, Darwish MS, Batt CA (2013) A real-time pcr-based microfluidics platform for the detection of cronobacter sakazakii in reconstituted milks. International Dairy Journal 33 (1):67–74 https://doi.org/DOI
17. Espitia PJP, Fuenmayor CA, Otoni CG (2019) Nanoemulsions: Synthesis, characterization, and application in bio-based active food packaging. Comprehensive Reviews in Food Science and Food Safety 18 (1):264–285 https://doi.org/DOI

18. Feng Y, Lee Y (2019) Microfluidic assembly of food-grade delivery systems: Toward functional delivery structure design. Trends in Food Science & Technology 86:465–478 https://doi.org/DOI
19. Ganesan P, Karthivashan G, Park SY, Kim J, Choi DK (2018) Microfluidization trends in the development of nanodelivery systems and applications in chronic disease treatments. International Journal of Nanomedicine 13:6109–6121 https://doi.org/DOI
20. Gao HW, Yan CL, Wu W, Li J (2020) Application of microfluidic chip technology in food safety sensing. Sensors 20 (6) https://doi.org/DOI
21. Gao W, Chen YP (2019) Microencapsulation of solid cores to prepare double emulsion droplets by microfluidics. International Journal of Heat and Mass Transfer 135:158–163 https://doi.org/DOI
22. Ge XH, Zhao H, Wang T, Chen J, Xu JH, Luo GS (2016) Microfluidic technology for multiphase emulsions morphology adjustment and functional materials preparation. Chinese Journal of Chemical Engineering 24 (6):677–692 https://doi.org/DOI
23. Geng Y, Ling S, Huang J, Xu J (2020) Multiphase microfluidics: Fundamentals, fabrication, and functions. 16 (6):1906357 https://doi.org/DOI
24. He F, Zhang MJ, Wang W, Cai QW, Su YY, Liu Z, Faraj Y, Ju XJ, Xie R, Chu LY (2019) Designable polymeric microparticles from droplet microfluidics for controlled drug release. Advanced Materials Technologies 4 (6) https://doi.org/DOI
25. He S, Joseph N, Feng S, Jellicoe M, Raston CL (2020) Application of microfluidic technology in food processing. Food & Function 11 (7):5726–5737 https://doi.org/DOI
26. Hsiao C-J, Lin J-F, Wen H-Y, Lin Y-M, Yang C-H, Huang K-S, Shaw J-F (2020) Enhancement of the stability of chlorophyll using chlorophyll-encapsulated polycaprolactone microparticles based on droplet microfluidics. Food Chemistry 306:125300 https://doi.org/DOI
27. Kennedy MJ, Ladouceur HD, Moeller T, Kirui D, Batt CA (2012) Analysis of a laminar-flow diffusional mixer for directed self-assembly of liposomes. Biomicrofluidics 6 (4) https://doi.org/DOI
28. Kim E, Lee H (2022) Mechanical characterization of soft microparticles prepared by droplet microfluidics. 60(11):1670–1699https://doi.org/DOI
29. Kim SH, Kim JW, Cho JC, Weitz DA (2011) Double-emulsion drops with ultra-thin shells for capsule templates. Lab on a Chip 11 (18):3162–3166 https://doi.org/DOI
30. Liu ZM, Yang Y, Du Y, Pang Y (2017) Advances in droplet-based microfluidic technology and its applications. Chinese Journal of Analytical Chemistry 45 (2):282–295 https://doi.org/DOI
31. Lorenceau E, Utada AS, Link DR, Cristobal G, Joanicot M, Weitz DA (2005) Generation of polymerosomes from double-emulsions. Langmuir 21 (20):9183–9186 https://doi.org/DOI
32. Maan AA, Schroën K, Boom R (2011) Spontaneous droplet formation techniques for monodisperse emulsions preparation – perspectives for food applications. Journal of Food Engineering 107 (3):334–346 https://doi.org/DOI
33. Maan AA, Nazir A, Khan MKI, Boom R, Schroën K (2015) Microfluidic emulsification in food processing. Journal of Food Engineering 147:1–7 https://doi.org/DOI

34. Marengo RC, Olivares ML, Berli CLA (2019) Generation of egg white/carrageenan microparticles by droplet-based microfluidics. Journal of Food Engineering 259:21–28 https://doi.org/DOI
35. Marze S, Algaba H, Marquis M (2014) A microfluidic device to study the digestion of trapped lipid droplets. Food & Function 5 (7):1481–1488 https://doi.org/DOI
36. Michelon M, Oliveira DRB, Furtado GD, de la Torre LG, Cunha RL (2017) High-throughput continuous production of liposomes using hydrodynamic flow-focusing microfluidic devices. Colloids and Surfaces B-Biointerfaces 156:349–357 https://doi.org/DOI
37. Michelon M, Huang Y, de la Torre LG, Weitz DA, Cunha RL (2019) Single-step microfluidic production of w/o/w double emulsions as templates for β-carotene-loaded giant liposomes formation. Chemical Engineering Journal 366:27–32 https://doi.org/DOI
38. Muijlwijk K, Berton-Carabin C, Schroen K (2016) Cross-flow microfluidic emulsification from a food perspective. Trends in Food Science & Technology 49:51–63 https://doi.org/DOI
39. Noviana E, Carrão DB, Pratiwi R, Henry CS (2020) Emerging applications of paper-based analytical devices for drug analysis: A review. Analytica Chimica Acta 1116:70–90 https://doi.org/DOI
40. Novo P, Moulas G, França Prazeres DM, Chu V, Conde JP (2013) Detection of ochratoxin a in wine and beer by chemiluminescence-based elisa in microfluidics with integrated photodiodes. Sensors and Actuators B: Chemical 176:232–240 https://doi.org/DOI
41. Opalski AS, Kaminski TS, Garstecki P (2019) Droplet microfluidics as a tool for the generation of granular matters and functional emulsions. Kona Powder and Particle Journal (36):50–71 https://doi.org/DOI
42. Pessi J, Santos HA, Miroshnyk I, Yliruusi J, Weitz DA, Mirza S (2014) Microfluidics-assisted engineering of polymeric microcapsules with high encapsulation efficiency for protein drug delivery. International Journal of Pharmaceutics 472 (1–2):82–87 https://doi.org/DOI
43. Ravanfar R, Comunian TA, Dando R, Abbaspourrad A (2018) Optimization of microcapsules shell structure to preserve labile compounds: A comparison between microfluidics and conventional homogenization method. Food Chemistry 241:460–467 https://doi.org/DOI
44. Ray R, Prabhu A, Prasad D, Garlapati VK, Aminabhavi TM, Mani NK, Simal-Gandara J (2022) Paper-based microfluidic devices for food adulterants: Cost-effective technological monitoring systems. Food Chem 390:133173 https://doi.org/DOI
45. Seo J, Lee LP (2004) Disposable integrated microfluidics with self-aligned planar microlenses. Sensors and Actuators B-Chemical 99 (2–3):615–622 https://doi.org/DOI
46. Shah RK, Shum HC, Rowat AC, Lee D, Agresti JJ, Utada AS, Chu L-Y, Kim J-W, Fernandez-Nieves A, Martinez CJ, Weitz DA (2008) Designer emulsions using microfluidics. Materials Today 11 (4):18–27 https://doi.org/DOI
47. Shang LR, Cheng Y, Zhao YJ (2017) Emerging droplet microfluidics. Chem Rev 117(12):7964–8040. https://doi.org/DOI
48. Shum HC, Lee D, Yoon I, Kodger T, Weitz DA (2008) Double emulsion templated monodisperse phospholipid vesicles. Langmuir 24 (15):7651–7653 https://doi.org/DOI

49. Shum HC, Abate AR, Lee D, Studart AR, Wang B, Chen C-H, Thiele J, Shah RK, Krummel A, Weitz DA (2010) Droplet microfluidics for fabrication of non-spherical particles. 31 (2):108–118 https://doi.org/DOI
50. Sugiura S, Nakajima M, Seki M (2000) Formation of monodispersed microspheres from microfabricated channel array. In: 1st Annual International IEEE-EMBS Special Topic Conference on Microtechnologies in Medicine & Biology, Lyon, France, Oct 12–14 2000. pp 283–287 https://doi.org/DOI
51. Taghizadeh-Behbahani M, Shamsipur M, Hemmateenejad B (2022) Detection and discrimination of antibiotics in food samples using a microfluidic paper-based optical tongue. Talanta 241:123242 https://doi.org/DOI
52. Tie S, Su W, Zhang X, Chen Y, Zhao X, Tan M (2021) Ph-responsive core–shell microparticles prepared by a microfluidic chip for the encapsulation and controlled release of procyanidins. Journal of Agricultural and Food Chemistry 69 (5):1466–1477 https://doi.org/DOI
53. Trofimchuk E, Nilghaz A, Sun S, Lu X (2020) Determination of norfloxacin residues in foods by exploiting the coffee-ring effect and paper-based microfluidics device coupling with smartphone-based detection. 85 (3):736–743 https://doi.org/DOI
54. Umbanhowar PB, Prasad V, Weitz DA (2000) Monodisperse emulsion generation via drop break off in a coflowing stream. Langmuir 16 (2):347–351 https://doi.org/DOI
55. Ushikubo FY, Oliveira DRB, Michelon M, Cunha RL (2015) Designing food structure using microfluidics. Food Engineering Reviews 7 (4):393–416 https://doi.org/DOI
56. Utada AS, Fernandez-Nieves A, Stone HA, Weitz DA (2007) Dripping to jetting transitions in coflowing liquid streams. Physical Review Letters 99 (9) https://doi.org/DOI
57. Visser CW, Kamperman T, Karbaat LP, Lohse D, Karperien M (2018) In-air microfluidics enables rapid fabrication of emulsions, suspensions, and 3d modular (bio)materials. Science Advances 4 (1) https://doi.org/DOI
58. Wang J, Li Y, Wang X, Wang J, Tian H, Zhao P, Tian Y, Gu Y, Wang L, Wang C (2017) Droplet microfluidics for the production of microparticles and nanoparticles. 8 (1):22 https://doi.org/DOI
59. Woolley AT, Mathies RA (1995) Ultra-high-speed DNA sequencing using capillary electrophoresis chips. Analytical Chemistry 67 (20):3676–3680 https://doi.org/DOI
60. Woolley AT, Hadley D, Landre P, deMello AJ, Mathies RA, Northrup MA (1996) Functional integration of pcr amplification and capillary electrophoresis in a microfabricated DNA analysis device. Analytical Chemistry 68 (23):4081–4086 https://doi.org/DOI
61. Zhang J, Zhang RT, Zhang YG, Pan Y, Shum HC, Jiang Z (2022) Alginate-gelatin emulsion droplets for encapsulation of vitamin a by 3d printed microfluidics. Particuology 64:164–170 https://doi.org/DOI
62. Zhang W, Abbaspourrad A, Chen D, Campbell E, Zhao H, Li Y, Li Q, Weitz DA (2017) Osmotic pressure triggered rapid release of encapsulated enzymes with enhanced activity. Advanced Functional Materials 27 (29):1700975 https://doi.org/DOI

63. Zhao CX, Chen D, Hui Y, Weitz DA, Middelberg APJ (2017) Controlled generation of ultrathin-shell double emulsions and studies on their stability. Chemphyschem 18 (10):1393–1399 https://doi.org/DOI
64. Zhao X, Li M, Liu Y (2019) Microfluidic-based approaches for foodborne pathogen detection. Microorganisms 7 (10) https://doi.org/DOI

Figures

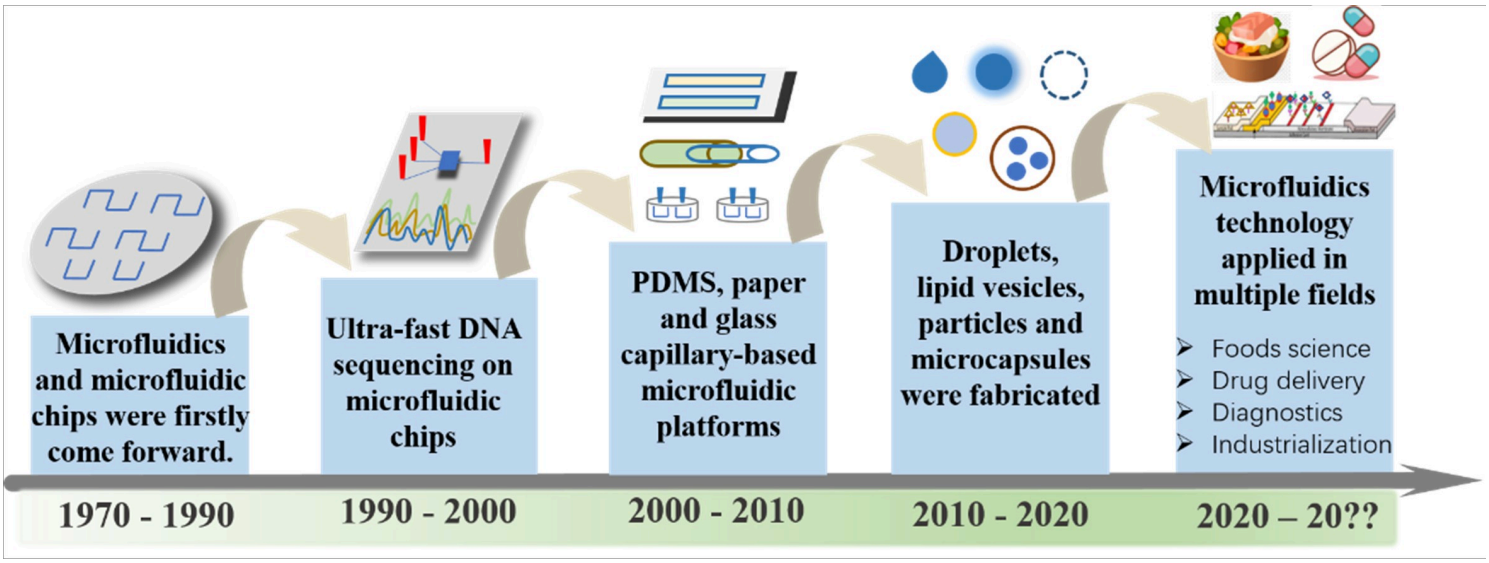


Figure 1

A brief schematic diagram of the history and development of microfluidics.

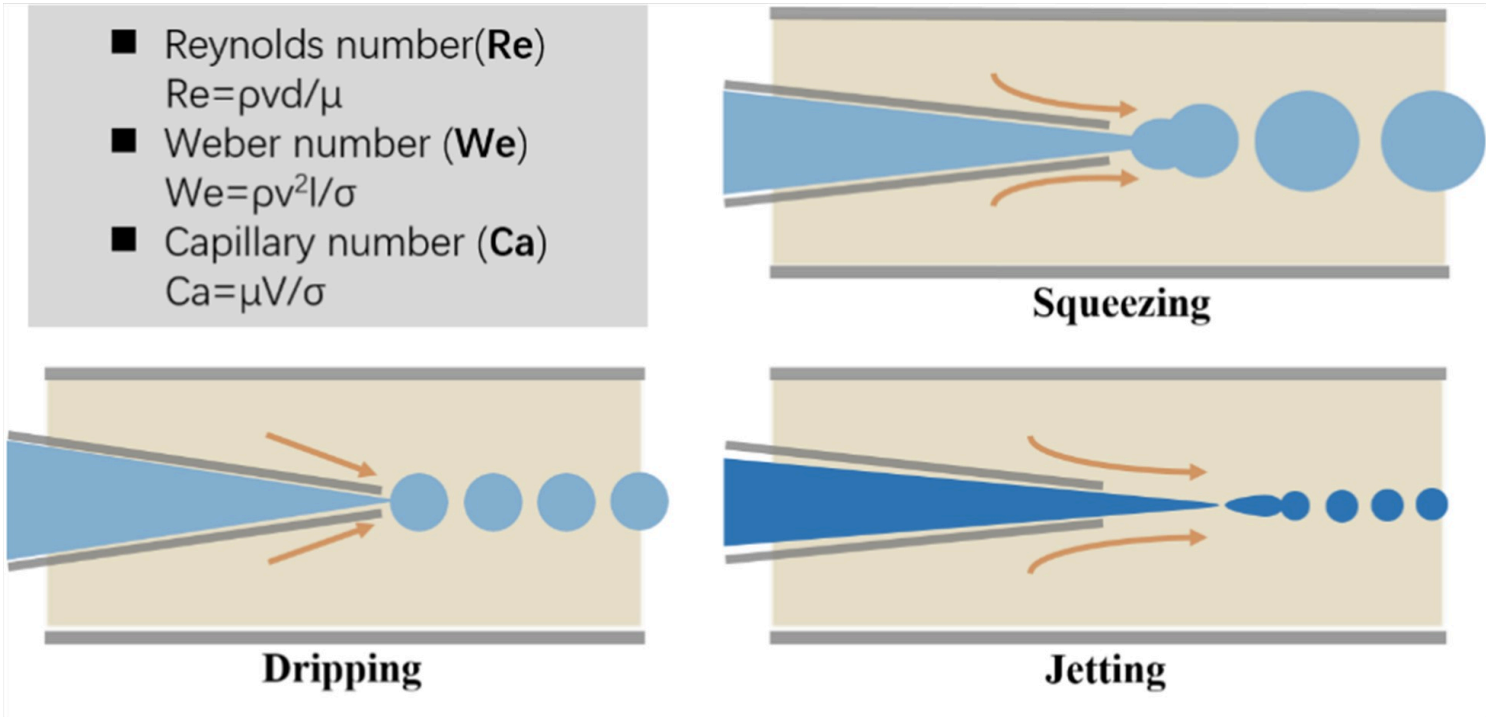


Figure 2

Typical flow parameters (Re, We, Ca) and modes of droplet formation (Squeezing, dripping, jetting).

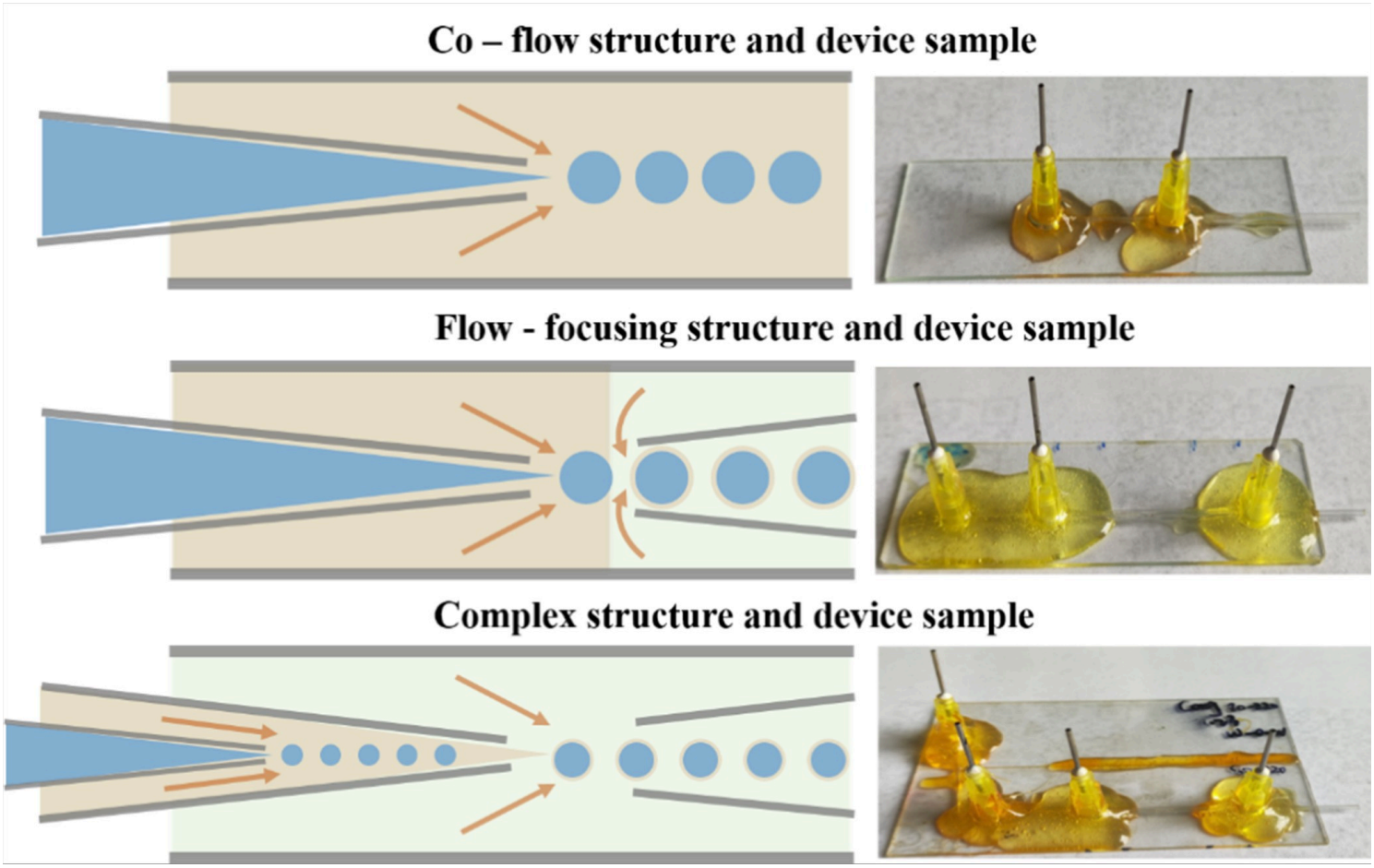


Figure 3

Microfluidic chips made by glass capillaries with different flow modes and channels.

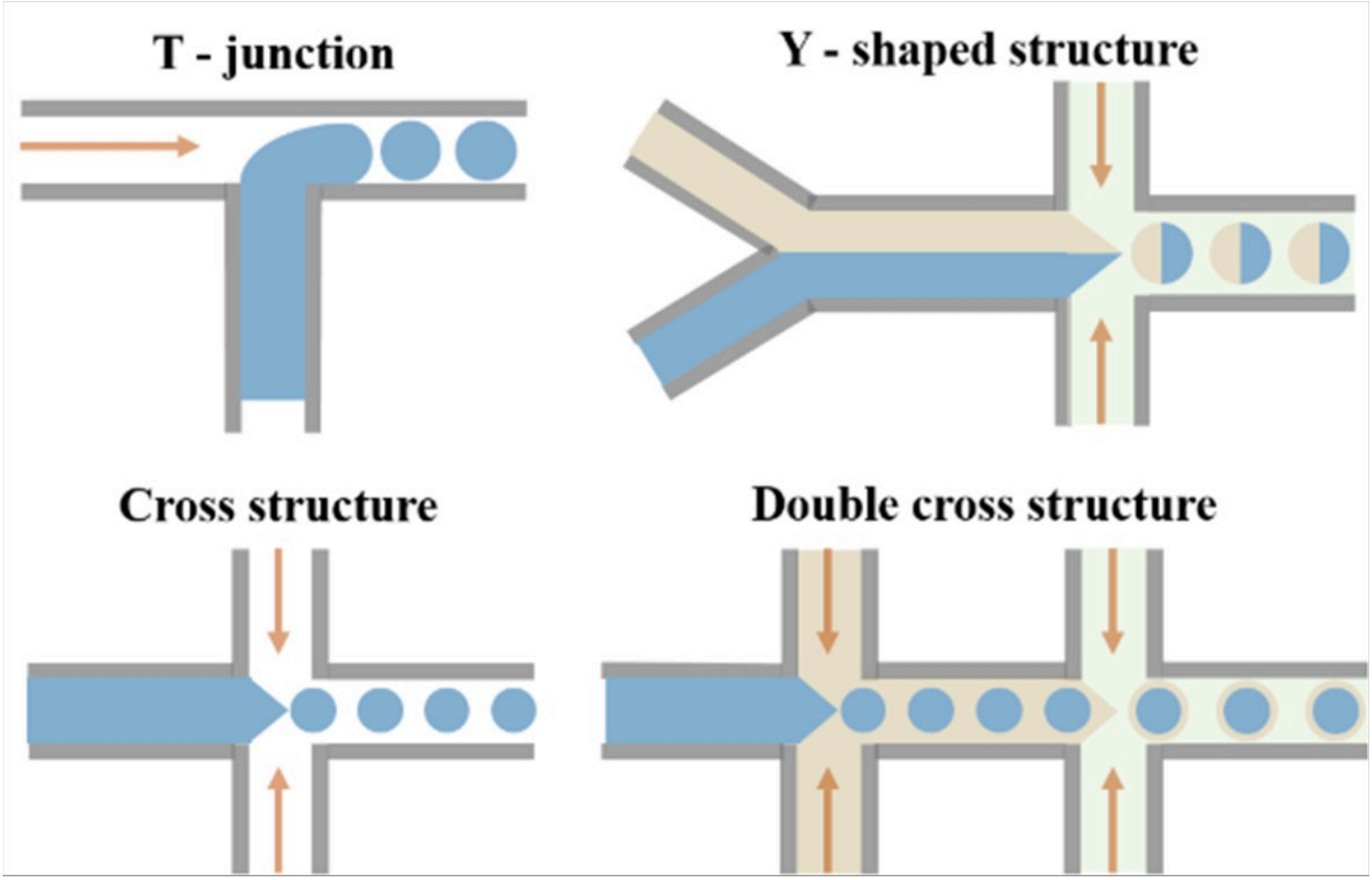


Figure 4

Four types of planar microfluidic chips. (a) T-junction, (b) Y-junction, (c) the cross-junction design and (d) the double cross-junction design.

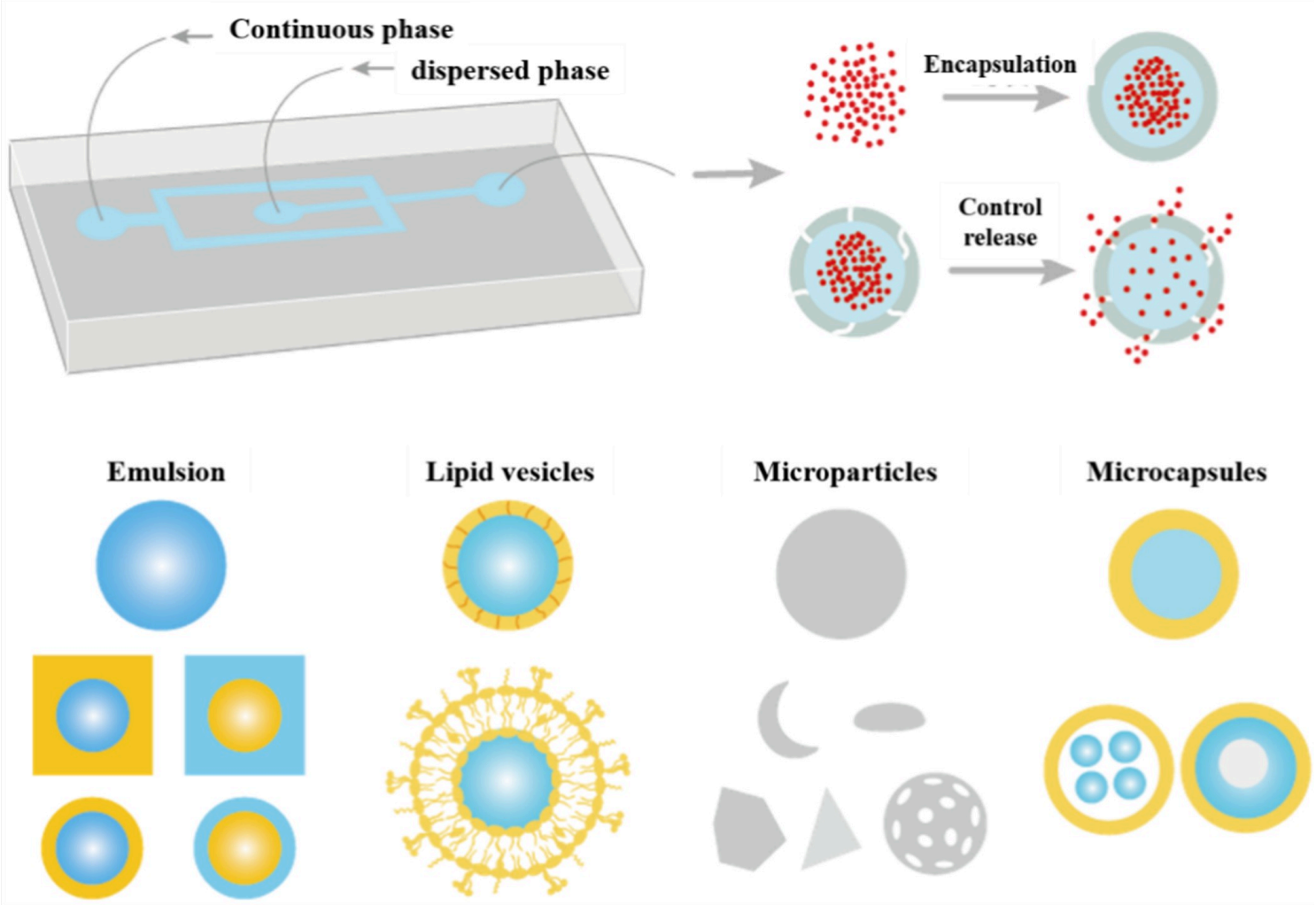


Figure 5

The applications of microfluidic products in food.