Trends in Food Science & Technology 46 (2015) 60–67

Contents lists available at ScienceDirect

Trends in Food Science & Technology

journal homepage: http://www.journals.elsevier.com/trends-in-food-science-and-technology

Review

Ultrasound applications for the extraction, identification and delivery of food proteins and bioactive peptides

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A R T I C L E I N F O

Article history:
Received 3 January 2015
Received in revised form
23 June 2015
Accepted 14 July 2015
Available online 17 July 2015

Keywords:
Ultrasound
Bioactive peptide
Digestion
Extraction
Drug delivery
Microencapsulation
ACE inhibitory peptide

A B S T R A C T

Bioactive peptides in foods can be obtained from plants, animal or marine sources. Bioactive peptides possess diverse biological activities such as opiate, antithrombotic, anti-hypertensive, immunomodulating, antilipemic, osteoprotective, antioxidative, antimicrobial, ileum contracting, anticariogenic and growth promoting properties. In general, peptide based drugs are physically and chemically unstable, have short *in vivo* half-lives and have low oral bioavailability. Ultrasound which is a novel, robust, green and rapid technology suitable for scale up, can enhance the efficiency of protein digestion, extraction, production and drug delivery of bioactive peptides. Ultrasound principally acts by generating bubble cavitation in the biological matrix. It has been extensively reported for extraction of proteins and peptides from natural products facilitating higher yields and rates of extraction. Ultrasound assisted encapsulation of peptide based drugs with biodegradable polymers can improve stability and bioavailability. Moreover, in sonophoresis applications, low-frequency ultrasound can be used to transport high molecular weight peptide drugs. This review paper summarizes key bioactive peptides, sources, structure, function and application of ultrasound for production and drug delivery of peptides.

1. Introduction

Recent developments in functional food research have generated renewed interest in bioactive compounds including bioactive peptides. The word "peptide" comes from the Greek term "πεπτιδια" translated as "small digestibles" or "digested" (Shahidi & Zhong, 2008). Biological activity of peptides were first reported by Mellander in 1950. In the last two decades there has been a strong interest in bioactive peptide identification and characterization. Researchers continue to investigate new sources, extraction methods and evaluate health benefits of bioactive peptides. Bioactive peptides are specific protein fragments that can alter body functions or conditions and may ultimately influence health positively (Korhonen & Pihlanto, 2006). Such peptides are inactive within the sequence of the parent protein and can be released by several hydrolysis techniques. Bioactive peptides have potential to help reduce the worldwide epidemic of chronic diseases affecting 58 million people annually (Sun, 2013). Currently the market for functional proteins and peptides is valued at $75 billion/year (Sun, 2013). Peptide based drugs sales are growing at a rapid pace with annual sales of $20 billion corresponding to 2% of the global drug market (Sun, 2013). Bioactive peptides from food proteins offer major potential for incorporation into functional foods and nutraceuticals. Major drivers for bioactive peptides drugs include their role as hormones, neurotransmitters and neuromodulaters, and low toxicity or non-toxicity of metabolic cleavage products. Challenges associated with the introduction of new peptide products include proteolytic degradation, fast clearance in the body, low solubility in water, immunogenicity (Bellmann-Sickert & Beck-Sickinger, 2010) and regulatory hurdles. Inactive or latent form of bioactive peptides in parent protein can be activated by proteolysis (Ryan, Ross, Bolton, Fitzgerald, & Stanton, 2011). Bioactive peptides may be produced by several methods: the most commonly employed are based on enzymatic hydrolysis by digestive enzymes derived from micro-organisms and fermentation of food proteins (Kim & Wijesekara, 2013). However other methods based on chemical hydrolysis or sub-critical water hydrolysis have also been widely researched in recent decades (Rogalinski, Herrmann, & Brunner, 2005).

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http://dx.doi.org/10.1016/j.tifs.2015.07.012

Sample preparation is one of the major limiting steps for rapid protein and peptide identification. Traditional methods of sample treatment are laborious, time consuming and involve use of chemical solvents (López-Ferrer et al., 2006). To reduce the time of sample preparation for protein and peptide identification, many measures have been investigated either separately or combined which include use of higher temperature during the digestion step, use of columns containing immobilized trypsin and addition of organic solvents. Use of novel techniques including high intensity ultrasound, microwave processing (Lopez-Ferrer, Capelo, & Vazquez, 2005) and high hydrostatic pressure (Toldrà, Parés, Saguer, & Carretero, 2011) have also been explored.

Ultrasound waves are sound waves that exceed the hearing limit of frequency of the human ear i.e. above 20 kHz. Ultrasound principally acts by generating bubble cavitation in the biological matrix. The various principal mechanisms of generation of bubble cavitation by ultrasound are shown in Fig. 1. Recent advances and developments have led to the introduction of more efficient and versatile ultrasound instrumentation which has expanded the potential applications of ultrasound in the food and biopharmaceutical industries (Awad, Moharram, Shaltout, Asker, & Youssef, 2012). The main applications of ultrasound in food biotechnology are outlined in Fig. 2. Application of ultrasound results in physico-chemical changes to proteins and peptides owning to/via sonochemical reaction, sonolysis of water, formation and collapse of cavitational bubble and microstreaming (O'Donnell, Tiwari, Bourke, & Cullen, 2010). Ultrasound is reported to be economically feasible and, meets process requirements including scale up (Chemat, Zill e, & Khan, 2011). The objective of this paper is to review reported applications of ultrasound for extraction, digestion, generation, encapsulation and controlled release of peptides and proteins. Bioactive peptides, their types, sources and biological activities are also outlined.

2. Bioactive peptides

2.1. Sources

Bioactive peptides in foods may be obtained from plants, animal or marine sources. Plant peptides, with molecular weight less than 10 kDa, can essentially be divided into two categories: bioactive peptides that are produced by selective action of peptidases on larger precursor proteins and degraded peptides that result from the activity of proteolytic enzymes during protein turnover. Bioactive peptides such as hypogin (peanut), angularin (adzuki bean), lunasin (soybean and barley) have been shown to have medicinal properties. Plant peptides also include glutathions and protease inhibitors such as Bowman–Birk inhibitors and mustard trypsin inhibitors (McGurl, Pearce, Orozco-Cardenas, & Ryan, 1992). Interestingly, most of the therapeutic peptides initially discovered were sourced from animal venoms and toxins (Redwan, 2009). Recently research has focused on discovery of new bioactive peptides from animal sources. Moreover, bio-functionalities and isolation procedures of previously discovered bioactive peptides are well documented in the literature. Peptides from animal sources possess biological activities such as antihypertensive, antioxidant, antimicrobial and antiproliferative activity (Ryan et al., 2011). Sources such as milk, egg and meat have been given special consideration due to their abundance in the human diet and documented biological activities. Enzymatic digestion is one of the common methods to obtain peptides from protein hydrolysates of meat products. In addition to this, fermentation of meat products is an alternate method to generate bioactive peptides by proteolytic enzymes during microbial fermentation (Arihara, 2006).

The marine environment provides half of the total global biodiversity. Marine bioresources have been investigated as a source of novel compounds for pharmaceutical and nutraceutical applications. Due to the competitive and aggressive nature of habitats, marine species develop specific and potent bioactive molecules (Aneiros & Garateix, 2004). Marine derived biologically active peptides are reported to have a range of functionalities including enzyme inhibition, mineral binding, immunomodulatory, antimicrobial, antioxidant, antithrombotic, hypocholesterolemic, and antihypertensive actions (Kim & Wijesekara, 2010). Moreover, fish protein hydrolysates and peptides thereof have been shown to have bioactive properties. Bioactive peptides and depsipeptides with functional properties have also been isolated from tunicates, sponges, soft corals, sea hares, nudibranchs, bryozoans, sea slugs, tunicates, sponges, mollusks and other marine organisms (Suarez-Jimenez, Burgos-Hernandez, & Ezquerra-Brauer, 2012).

2.2. Structure and function

Peptides are formed by condensation of two or more amino acids. Peptides are classified into ribosomal and non-ribosomal

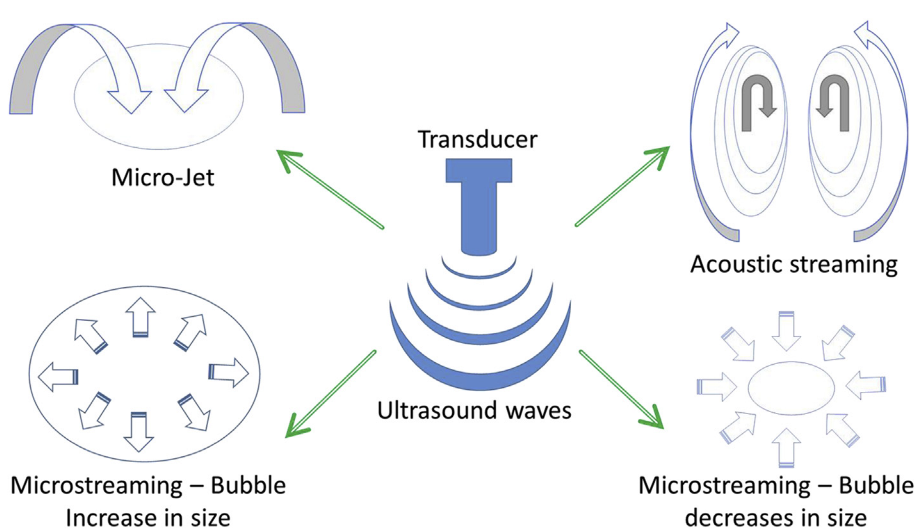

Fig. 1. Mechanism of bubble cavitation phenomenon.