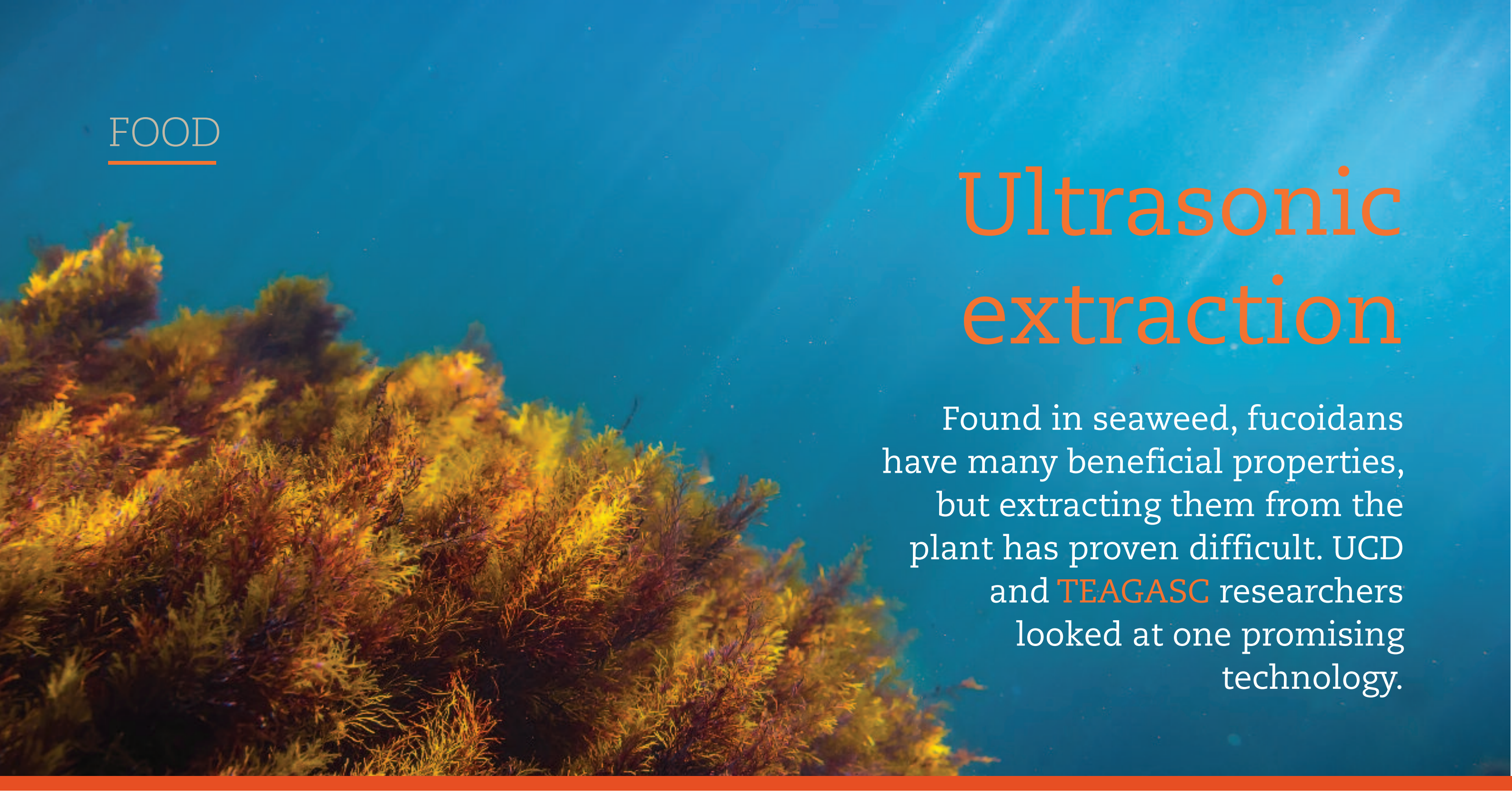

Ultrasonic extraction

Found in seaweed, fucoidans have many beneficial properties, but extracting them from the plant has proven difficult. UCD and TEAGASC researchers looked at one promising technology.

Fucoidans are sulfated water-soluble heteropolysaccharides found in brown seaweed and demonstrate a variety of biological activities including antioxidant, antimicrobial, antiviral, antitumour, anti-proliferative and immunostimulatory activities (Garcia-Vaquero *et al.*, 2017). Fucoidans are composed of fucose, glucose, xylose, galactose, mannose, glucuronic acid and sulfate substituents (**Figure 1**). They have been investigated in recent years for their potential applications in pharmaceuticals, food and animal feeds. Fucoidans are present in the cell wall of brown seaweed associated with proteins, alginates and other molecules (**Figure 2**), and play a crucial role in the protection of the seaweed against environmental challenges. However, the composition, activity and structure of fucoidans depends on the seaweed species, harvesting season, geographic location, tissues, growth stage, environmental conditions, molecular weight, monosaccharide composition, sulfate content, position of the sulfated ester group, as well as the extraction process. Fucoidan is a high molecular weight compound, hence its application in drug delivery is limited. Therefore, more research is focused on highly active low molecular weight fucoidans (LMWF) and the substructures of these large macromolecules. These LMWFs can be obtained by partial acid hydrolysis or by degradation of large fucoidan molecules using innovative techniques such as microwave or ultrasound during the extraction process. These processes may cause structural modifications, such as desulfation, debranching or degradation, which can result in distinct biological properties compared with the intact fucoidans.

Extraction of fucoidan

The extraction of fucoidan in industry is mainly performed using conventional approaches, including the use of multiple and large volume of solvents (water, dilute acid or dilute alkali, etc.) and a wide range of extraction conditions including high temperatures (40-100°C) and long times of extraction (three to 24 hours). The fucoidan extracts are normally generated by applying these extraction conditions, one or multiple times over the same seaweed residue to achieve the desired high yield. Scientists are now exploring the use of innovative technologies to increase the efficiency of the extraction of fucoidan in terms of yield, time and cost of extraction, while lowering the consumption of energy and using more environmentally friendly solvents. In the last decade, microwave-assisted extraction (MAE), enzyme-assisted extraction (EAE) and ultrasound-assisted extraction (UAE) have been successfully used for extraction of numerous biologically active compounds from a wide variety of natural resources. However, these novel extraction protocols developed using innovative technologies should be optimised not only to achieve high yields, but also to maintain the biological activities of biomolecules (Garcia-Vaquero *et al.*, 2017). In seaweed, multiple extraction technologies have been used to extract fucoidan, but ultrasound could provide an economically feasible technique with potential for scale-up.

Ultrasound-assisted extraction

UAE is based on the application of sound waves that migrate via a series of compression and rarefaction cycles induced on the molecules of the solvent medium they travel through. During these cycles, small bubbles filled with vapours are produced, which grow to a certain size and collapse periodically, transforming the sound waves into mechanical energy, which disrupts the algal cell wall and facilitates the extraction of bioactive compounds. The formation of small bubbles in a liquid is defined as cavitation. Cavitation generates high-velocity inter-particle collisions and turbulence, which initiate the solid-liquid phenomenon including surface peeling, erosion, and particle breakdown. These effects increase the mass transfer by eddy and internal diffusion mechanisms, and improve the efficiency of extraction, expediting the release of fucoidans from the seaweed matrix (Kadam *et al.* 2015).

Low-frequency ultrasound (<200kHz) produces large but unstable bubbles which collapse during the compression cycle, releasing large amounts of heat and shockwaves. This creates high localised temperatures (around 5,000K) and pressure jets, while high-frequency ultrasound (>1MHz) generates tiny but more stable bubbles, which open and close, creating localised microstreaming effects. However, the high temperature and pressure jets generated from low-frequency unstable bubbles is helpful to burst the cell structures releasing intracellular components into the medium. Therefore, low-frequency ultrasound, also known as UAE, has been largely explored for the extraction of fucoidans from seaweed. During

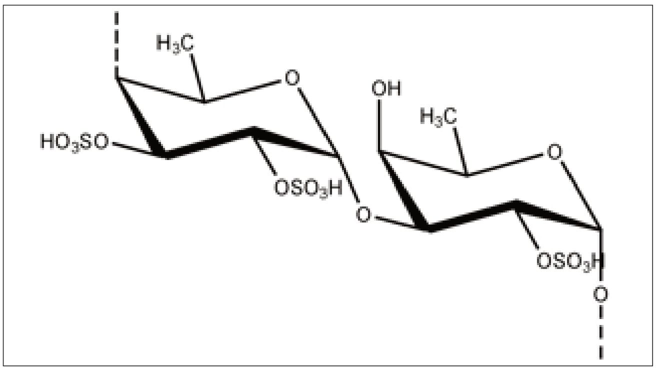

FIGURE 1: Chemical structure of fucoidan.

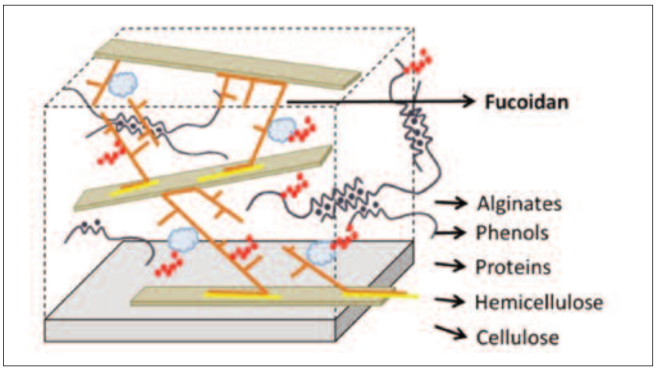

FIGURE 2: Fucoidan and other molecules integrating the cell wall structure of brown seaweeds.

UAE, most of the polysaccharides (including fucoidans) are released from the degraded cell wall at the early stage of ultrasonic processing with suitable ultrasonic power. The acidic or alkaline medium makes the algal cell wall porous and wrinkled, leading to increased yields at low temperature (<60°C) over a short time (<3 hours), while a high temperature (around 90°C) and a longer time (around five hours) cause fucoidan degradation and lower sulfate contents, leading to structural alterations and reduced biological activity.

The application of ultrasound is simple, cost-effective and more efficient than other traditional extraction techniques due to its high extraction yields and short application times. UAE can be performed by using ultrasonic bath, probe, plates or tubular devices populated with small transducer ceramics. However, a number of parameters such as ultrasonic frequency, power, intensity, shape and size of the ultrasonic device/probe, solvents, time and temperature, greatly influence the extraction efficiency. Moreover, UAE can be combined with other technologies, e.g., UAE with microwave, to achieve higher yields of compounds if the molecules are resistant to heat.

Future prospects

The production of food and pharmaceutical products must comply with good manufacturing practices (GMP). Therefore, reproducible cultivation and harvesting of seaweed must be established. Many traditional methods, as well as innovative technology-based protocols, are proposed for the extraction of fucoidans from seaweeds. Most of the studies are focused on obtaining high yields of fucoidan or polysaccharides in general, without optimising the technologies or extraction parameters. A promising approach using UAE to generate lower molecular weight fucoidan fractions that conserve the sulfate content and sugar backbone is required. Thus, successful optimisation of UAE parameters to control the degradation process, as well as beneficial biological activities, is important for the production of the appropriate active fucoidan at the required scale.

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