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The foodome of bivalve molluscs: From hedonic eating to healthy diet

Violetta Aru*, Bekzod Khakimov, Klavs Martin Sørensen, Søren Balling Engelsen

Department of Food Science, University of Copenhagen, Rolighedsvej 26, 1958 Frederiksberg C, Denmark

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ABSTRACT

Bivalve molluscs, including oysters and scallops, are hedonic foods that have been a valuable source of vitamins, minerals and proteins in the human diet since the Stone Age. Despite being rich in beneficial compounds, it is still debatable whether bivalves should be regarded as a healthy food since they can accumulate harmful microorganisms, and toxic compounds from the surrounding environment. Currently, there is still no in-depth understanding of the ultimate effect of bivalve consumption on humans. The use of advanced foodomics approaches is beginning to provide a more detailed characterisation of the beneficial and deleterious compounds in these seafood products. In addition to defining bivalve molluscs within an international dietary framework, this review highlights the major nutritional components of their metabolome (foodome) with a focus on several groups of toxicants whose presence can negatively offset their nutritional value. An overview of metabolomics applications to the study of bivalve molluscs is included.

1. Introduction

Increased awareness of wellness as a function of healthy eating habits and lifestyle is currently driving consumers' interest in seeking for functional foods that, besides providing basic nutrients, offer additional health benefits (Shahidi, 2004). Common functional foods include fruits, vegetables, whole grains, as well as fortified foods and beverages (Ozen et al., 2012). Several beneficial substances can be found in foods including ω-3 fatty acids (Swanson et al., 2012), dietary fibers (*i.e.* β-glucans) (Wood, 2007), vitamins (*i.e.* tocopherols) (Bou Ghanem et al., 2017), minerals (Soetan et al., 2010), and polyphenols (*i.e.* resveratrol) (Khakimov and Engelsen, 2017).

Today seafood is an important part of several dietary patterns as it contains many beneficial substances (Kaur et al., 2012). Among seafood products, marine bivalves are hedonic foods whose inclusion in a dietary pattern helps provide an adequate intake of long-chain poly unsaturated fatty acids (LC-PUFAs), vitamins (*i.e* vitamin D and E), minerals (*i.e.* calcium and potassium) and essential amino acids (Soccol and Oetterer, 2003). Despite the above-mentioned nutritional properties, several potential hazards can be found in bivalves, such as heavy metals, marine toxins, organic pollutants and microorganisms (Hellberg et al., 2012). Balanced diets have therefore become important tools for maximising the benefits and minimising risks related to bivalve shellfish consumption.

Generally, two different paths are explored when promoting healthy foods (Bere and Brug, 2009). The first focuses on the specific composition of food in terms of beneficial bioactive compounds and thus leads to nutrient-specific recommendations. In the second, the nutrients in a food item are seen in a more holistic context and the interactions with other food components and hazardous compounds are taken into account. Within this framework, holistic analytical approaches are essential tools for the global assessment of risks and benefits related to food intake (Hellberg et al., 2012).

In recent years, the *omics* sciences have emerged as alternative analytical tools in nutrition research. Among omics disciplines, metabolomics has one peculiar advantage: metabolic fluxes are not just regulated by gene expression alone, but by complex feedback mechanisms and regulatory networks that are decoupled from gene expression and play a prominent role in metabolome modulation (Patti et al., 2012). Therefore, being focused on the study of the overall low molecular weight metabolites (> 1500 Da), metabolomics reflects more closely the physiology of the biological systems at a functional level, providing a realistic snapshot of the phenotype of the organism under investigation (Fiehn, 2002). The metabolomics approach is rapidly developing into the research area called *foodomics* in which omics sciences are applied to investigate and resolve crucial issues in the fields of food and nutritional sciences (Brennan, 2013; Khakimov et al., 2016; Savorani et al., 2013).

The rapid expansion of metabolomics applications owes a great deal to major advances in analytical platforms (Zhang et al., 2012). Several analytical techniques are currently used for metabolites identification and quantification. Mass spectrometry (MS) and nuclear magnetic resonance spectroscopy (NMR) have always played a prominent role in metabolomics studies (Pan and Raftery, 2007). They have been

* Corresponding author at: Chemometrics and Analytical Technology, Dept. Food Science, University of Copenhagen, Rolighedsvej 26, 1958 Frederiksberg C, Denmark.
E-mail address: violetta@food.ku.dk (V. Aru).

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demonstrated to complement each other in terms of sensitivity and reproducibility and their combined use has been reported in several metabolomics applications, from biomarkers identification to environmental monitoring studies (Putri et al., 2013).

The present review provides an overview of the deleterious and beneficial substances present in major aquaculture industry products, namely bivalve molluscs, citing examples of the most relevant metabolomics and foodomics studies.

2. Bivalves in a dietary framework

Seafood is considered as an important component of gourmet meals. Several types of diets include seafood as one of the major food items providing high quality proteins, amino acids, vitamins and ω-3 fatty acids. Marine bivalves are one of the most appreciated seafood delicacies, with mussels, scallops, clams and oysters being widely commercialised for human consumption. The production of marine bivalves plays a prominent role in the aquaculture industry. As registered by the Food and Agriculture Organization (FAO) of the United Nations, 632, 000 t of bivalves, including fed and non-fed species, were produced in Europe in 2014 (FAO, 2016).

Marine bivalves have always played an important role in two international eating patterns: the Mediterranean diet and the Paleo diet. However, the motivations behind these diets are different: while the Mediterranean diet promotes a wide variety of food intake by encouraging the consumption of whole/natural foods and increased fruit and vegetable intake, the rationale behind the Paleo diet is that foods that were available during the evolution of primates are healthier than more recently introduced ones that the human digestion system was not designed to metabolise (Jew et al., 2009). Moreover, evidence on the crucial role of some of the food components of the Paleo diet in the evolution of different anatomical features of human beings have been reported. Recent research on the relationship between human evolution and water environments has demonstrated that the expansion of the human brain required a plentiful source of LC-PUFAs, such as seafood products (Jew et al., 2009). Membranes rich in LC-PUFAs are necessary to construct tissues that have high rates of signal transfer and data processing such as those constituting the cerebral tissues and nervous system (Guesnet and Alessandri, 2011). Besides their putative role in human evolution, LC-PUFAs are considered important “drivers” of human health (Ruxton et al., 2004).

3. The foodome of bivalve molluscs: beneficial and deleterious compounds

Bivalve molluscs are considered by some as a healthy food choice as they are a valuable source of proteins and provide long-chain ω-3 fatty acids, which are important functional compounds (Hellberg et al., 2012). However, bivalve consumption plays a significant part in human poisoning as they can be the vehicle for anthropogenic and environmental toxicants (Sioen et al., 2009). This “food chain” route of contamination is especially important for chemicals (*i.e.* trace metals, dioxin-like compounds and pesticides) and biological contaminants (*i.e.* microorganisms and algal toxins). Bivalve molluscs are filter-feeders, feeding mainly on a wide range of phytoplankton species some of which produce toxins (Ciminiello and Fattorusso, 2006) and can accumulate pollutants from the surrounding environment (Fig. 1). Due to the risks posed to human health, concentrations of toxicants in bivalves are regulated under European legislation (Commission regulation (EU) 2015/2285 of 8 December 2015) which provides guidelines for the farming of bivalve molluscs and defines specific rules for the control of seafood quality.

The following sections provide an overview of the major components of the foodome of bivalve molluscs in terms of beneficial and deleterious compounds, with a focus on the environmental factors (natural and anthropogenic) that may affect their molecular composition.

3.1. Amino acids

The amino acid load of bivalves consists of both essential and non-essential amino acids. The essential amino acids phenylalanine, valine, threonine, tryptophan, methionine, leucine, isoleucine, lysine, and histidine are normal components of the metabolome of bivalves (Gosling, 2015). Bivalve molluscs are also rich in taurine (Fig. 2a), a sulfur-containing amino acid that is present in all animal species (Lambert et al., 2015) and has several biological functions, from antioxidant protection (Aruoma et al., 1988) to body detoxification (Huxtable, 1992). Along with free α-amino acids, taurine is one of the major intracellular osmotic components involved in osmotic regulation in marine bivalves (Yancey, 2005). In these organisms, organic osmolytes can be upregulated or down regulated to adjust the osmotic pressure of cells to match the conditions of the aquatic environment.

3.2. Fatty acids

Marine fish and shellfish remain one of the principal sources of LC-PUFAs which are functional compounds considered essential to human health (Heideman Soccol and Oetterer, 2003). LC-PUFAs include, but are not limited to, alpha linolenic acid (ALnA), the main precursor of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), and alpha linoleic acid (ALA) the precursor of arachidonic acid (AA) (Fig. 2b). Among LC-PUFAs, DHA, the dominant ω-3 fatty acid in the human brain, plays a prominent role in the central nervous system (Guesnet and Alessandri, 2011). Despite the important biochemical functions of this fatty acid, humans’ capacity to synthesise DHA *ex novo* is limited and dietary supplements are required (Guesnet and Alessandri, 2011).

3.3. Carbohydrates

Carbohydrates are widely distributed in marine bivalves in the forms of mono- and disaccharides (*i.e.* glucose and sucrose, respectively) and polysaccharides (*i.e.* glycogen) that can fulfil antioxidant (Peshev and Van den, 2013), signalling (Yadav et al., 2014), transport (Lemoine et al., 2013), and storage functions (Bihmidine et al., 2013). They are mainly used as an energy store to overcome a shortage of food such as during winter and gametogenesis (Fearman et al., 2009).

Seven-carbon (7-C) sugars and sugar alcohols are monosaccharides that are widely distributed in higher plants, algae, fungi and bacteria (Cowan, 2017). Among the best studied 7-C sugars are mannoheptulose, volemitol, lamntitol and its epimer mytilitol (Cowan, 2017). The latter was first identified in mussels (Daniel and Doran, 1926) (Fig. 2c).

3.4. Toxins

Bivalve molluscs have the potential to accumulate particulate and dissolved matter from the water column including naturally-occurring toxins deriving from harmful algal blooms (Garthwaite, 2001). Marine biotoxins in particular pose a significant risk to humans when accumulated in the tissues of edible shellfish. One of the prevalent groups of toxins are the okadaic acid (OA) group toxins. These toxins are produced by several marine dinoflagellates which represent one of the major phytoplankton constituents. Diarrheic shellfish poisoning (DSP) is the illness caused by the ingestion of shellfish contaminated by these toxins (Johnson et al., 2016). Similarly, domoic acid (DA), the main toxin associated with amnesic shellfish poisoning (ASP), is produced as a consequence of naturally occurring blooms of the diatom Pseudo-nitzchia (Jeffery et al., 2004). Paralytic shellfish poisoning (PSP) toxins are potent neurotoxins produced by marine dinoflagellates (Etheridge, 2010). High concentrations of saxitoxin (STX), one of the toxins responsible for PSP, can potentially lead to human fatality (Etheridge,