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# Meat proteome as source of functional biopeptides

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ABSTRACT

Food-derived compounds have been linked with decreased risk of developing chronic health conditions. The interest in the development of functional biopeptides from food proteins can be attributed to increasing consumer demand for safe health-promoting agents. The meat proteome, although not as widely investigated as dairy, fish or plant proteins, contains peptide sequences with a variety of beneficial health effects particularly antihypertensive property as well as other health-promoting functions such as antioxidant, antithrombotic, anticancer, immunomodulatory and antimicrobial activities. Despite the prospects, current literature indicates dearth of extensive information on validation of the physiological functions of meat-derived biopeptides in animal models and human subjects. Moreover, bioinformatic analysis has indicated the possibility of generating a myriad of biopeptides during endogenous metabolism of dietary meat proteins, and through the use of food-grade exogenous proteases. Consequently, there is a strong need to explore the meat proteome as precursor of functional biopeptides for the development of commercial functional foods and nutraceuticals.


## 1. Introduction

Food and health are inextricably linked since food components possess direct positive and negative impacts on metabolic processes and physiological functions. Many of the current health problems faced by civilization such as cardiovascular disease, diabetes and cancer have direct linkages with human dietary patterns. The risk of developing coronary heart disease and stroke has been correlated with excess intake of saturated dietary fat (Bhupathiraju & Tucker, 2011) whereas hypertension can be elicited by overconsumption of dietary sodium (He & MacGregor, 2009). Poor dietary pattern, such as intake of high amounts of sugars and saturated fats, increases the risk of developing type II diabetes characterized by high blood sugar levels due to insulin resistance (Gallagher, LeRoith, & Karnieli, 2010). Cancer, inflammatory and neurodegenerative diseases can be induced by oxidative stress, where the amount of free radicals and reactive oxygen species overpower the physiological antioxidant capability leading to oxidative damage of cellular DNA, proteins and lipids (Ames, Shigena, & Hegen, 1993; Reuter, Gupta, Chaturvedi, & Aggarwal, 2010). Many of these human health conditions can be managed using a variety of pharmaceutical drugs. However, chemotherapy can cause serious adverse effects. For instance, several hypertension treatments can cause a variety of electrolyte imbalances such as hyponatremia, hyper- and hypokalemia, hypercalcemia (Liamis, Millionis, & Elisaf, 2008), and angioedema (Finley, Silverman, & Nunez, 1992). Statins, the most popular and commonly prescribed drug class for high cholesterol, are associated with various myopathies and renal failure (Sakaeda, Kadoyama, & Okuno, 2011), and potentially liver damage (Björnsson, Jacobsen, & Kalaitzakis, 2012). Therefore, there is increased interest in the discovery of safer health intervention agents, such as functional foods, that can help to alleviate or prevent these health conditions. The development of functional biopeptides from the diverse food proteome is a viable method of adding functional value to human foods. This can be attributed to increasing consumer demand for natural health products, as treatments derived from natural sources have low toxicity and fewer incidences of adverse side effects compared to drugs.

Numerous studies in the literature have reported several health-related activities of biopeptides derived from food protein sources of animal origin such as dairy and egg proteins (Haque, Chand, & Kapila, 2009; Miguel & Aleixandre, 2006). To date, the most widely investigated health-promoting function of these peptides has been on the reduction of blood pressure during hypertension. These effects, plus antioxidant, opioid, antimicrobial and other activities, have also been reported for peptides derived from a variety of plant- and marine-based food protein sources (Choi, Sabikhi, Hassan, & Anand, 2012; Espitia et al., 2012; Martinez-Maqueda, Miralles, Recio, & Hernández-Ledesma, 2012; Sarmadi & Ismail, 2010; Udenigwe & Aluko, 2012a; Udenigwe et al., 2012; Walther & Sieber, 2011). A number of research investigations are currently focusing on the development of functional biopeptides from meat proteins. Animal agriculture leads to the production of primary food products for human nutrition and secondary byproducts of negligible economic value to the industry. For example, the muscles and other tissues of animals may contain high amounts of collagen, which affects their usefulness

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for human consumption (Lepetit, 2008) due to the toughness of the meats. Moreover, disposal of undesirable animal by-products may negatively affect the environment due to associated carbon footprints. Consequently, there is need for value addition to renewable animal by-products for economic and environmental sustainability. Furthermore, there is a continuous interest in innovative and leading edge expansion of market applications of meat-based foods that are used primarily in human nutrition. The proteins present in food products of animal origin contain peptide sequences that possess experimentally validated and potential health functions when liberated from the parent proteins. This paper reviews the current state of knowledge and future opportunities regarding utilization of the diverse protein resources of meat as precursors of health-promoting biopeptides.

## 2. The meat proteome

Meat is a major source of high quality dietary proteins for primary metabolic processes due to their constituent amino acids. The skeletal muscles form a major part of meats and are composed of large protein aggregates arranged to form the thick and thin filaments, which contain myosin and actin, respectively as major components (Huff-Lonergan, Zhang, & Lonergan, 2010). Attached to actin in the thin filaments are proteins troponin and tropomyosin, which play regulatory roles in the myofibrillar structure. The thick and thin filaments are arranged to form the functional sarcomere unit, which forms the myofibrils and subsequently the myofibers; the myofibers then assemble to form the muscle fibers (Ryan, Ross, Bolton, Fitzgerald, & Stanton, 2011; Vercruysse, Van Camp, & Smagghe, 2005). Proteomic studies have indicated that there could be more than 65 proteins and possibly isoforms within the sarcomere unit (Fraterman, Zeiger, Khurana, Wilm, & Rubinstein, 2007; Huff-Lonergan et al., 2010). At the molecular level, myosin is composed of two heavy chains (MHC) and 4 light chains (MLC) whereas actin (F-actin) is a polymer of G-actin units (Vercruysse et al., 2005). Other muscle mega-proteins, titin (connectin) and nebulin, are structurally associated with myosin and actin, respectively, and play supporting roles in the muscle unit (Huff-Lonergan et al., 2010). These myofibrillar proteins are involved in the functioning of the skeletal system during contraction of striated muscles. In addition, meat muscles contain several proteins in the sarcoplasm that play transport, catalytic and regulatory roles including glycolytic enzymes, myoglobin, and proteins found within muscle mitochondria, sarcoplasmic reticulum and lysosomes. Detection of the low-abundant proteins is often hindered by the predominant myofibrillar proteins but this can be circumvented by appropriate fractionation (Hollung, Veiseth, Jia, Færgestad, & Hildrum, 2007). In a proteomic study, Doherty et al. (2004) reported that the pectorialis muscle of growing layer chicken contained several proteins with diverse structural and functional properties. Table 1 shows a list of the soluble proteins identified in chicken breast meat by 2D-gel electrophoresis and matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry; the numbered protein spots from the gel electrophoresis are shown in Fig. 1. Although the presence and accumulation of proteins in muscle meats may be dependent on the developmental stage of the animals due to dynamic protein synthesis and degradation (Hollung et al., 2007), as indicated by the protein spots in Fig. 1, the amino acid sequence diversity of the proteins in Table 1 as found in UniProtKB/Swiss-Prot database (identified by accession numbers) enhances their potential use as precursors of functional biopeptides.

The connective tissue is made up of mostly fibrillar collagen, a large structural protein that can also serve as precursor of bioactive peptides, having high frequencies of antihypertensive, antithrombotic and dipeptidylpeptidase IV inhibitors within its primary sequence (Minkiewicz, Dziuba, & Michalska, 2011). Collagen contains high amounts of glycine and proline residues, which may impart unique properties to the protein and its polypeptide fragments. For instance, peptides with relatively high amounts of proline are generally resistant to further proteolysis by intestinal epithelial enzymes (Aito-Inoue, Lackeyram, Fan, Sato, & Mine, 2007). Moreover, the presence of high amounts of glycine was associated with enhanced antioxidant activity

**Table 1**
Chicken skeletal muscle proteins identified by proteomics approach[a].

| Spot no.[b] | Identification | Accession no. | Spot no.[b] | Identification | Accession no. |
|---|---|---|---|---|---|
| 1 | Serum albumin | P19121 | 27 | Casein kinase 1 α-isoform | P70065 |
| 2 | β-Enolase | P07322 | 28 | Myoglobin | P02189 |
| 3 | Creatine kinase | P00565 | 29 | Fatty acid-binding protein | P80565 |
| 4 | Phosphoglycerate mutase | P18669 | 30 | Actin polymerisation inhibitor | Q00649 |
| 5 | Triosephosphate isomerase | P00940 | 31 | Protein kinase C inhibitor | Q9I882 |
| 6 | Apolipoprotein A1 | P08250 | 32 | Aldolase C | P53449 |
| 7 | Ovotransferrin | P02789 | 32 | β-Actin | P53478 |
| 8 | Adenylate kinase isozyme 1 | P05081 | 33 | α-Enolase | P51913 |
| 9 | L-Lactate dehydrogenase A-chain | P00340 | 34 | T-complex protein | P48643 |
| 10 | Nucleoside diphosphate kinase | O57535 | 35 | Citrate synthase | P23007 |
| 11 | Phosphoglucomutase | P00949 | 36 | Tubulin β-7 chain | P09244 |
| 12 | Phosphoglycerate kinase | P51903 | 37 | Tubulin α-chain | P02552 |
| 13 | Pyruvate kinase | P00548 | 38 | Vimentin | P48674 |
| 14 | Heat shock protein 90-α | P11501 | 39 | PIT 54 | Q98TD1 |
| 15 | Elongation factor 2 | Q90705 | 40 | Endoplasmin | P08110 |
| 16 | Glycerol-3-phosphate dehydrogenase | P13707 | 41 | Immunoglobulin heavy binding protein | Q90593 |
| 17 | Glyceraldehyde 3-phosphate dehydrogenase | P00356 | 42 | L-Lactate dehydrogenase B-chain | P00337 |
| 18 | Cofilin | P21566 | 43 | L-Lactate dehydrogenase M-chain | P06151 |
| 19 | Hemoglobin α-D chain | P02001 | 44 | Destrin | P18359 |
| 20 | Hemoglobin α-A chain | P01994 | 45 | Myosin regulatory light chain 2 | P97457 |
| 21 | Apolipoprotein AIV | O93601 | 46 | Transthyretin | P27731 |
| 22 | c-Jun *N*-terminal kinase 2 | P79996 | 47 | Fructose bisphosphate aldolase | P05064 |
| 23 | Glycogen phosphorylase | P00489 | 48 | Vitamin D binding protein | Q9W6F5 |
| 24 | Fructose-1,6-bisphosphatase | Q9I8D3 | 49 | Carbonic anhydrase | Q9ERN8 |
| 25 | α-Actin | P02568 | 50 | Aldehyde dehydrogenase | P27463 |
| 26 | Myosin light chain I | P05977 | 51 | Guanine nucleotide binding protein | O73819 |
| 26 | Tropomyosin α-chain | P02559 | 52 | Annexin V | P17153 |
| | | | 53 | Adenosyl homocysteinase | P51893 |

[a] Adapted from Doherty et al. (2004) with permission from John Wiley and Sons.
[b] Spot number of identified proteins with reference to 2D-electrophoresis gels in Fig. 1.

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