Meretrix Meretrix: Active Components and Their Bioactivities

Wenyan Xie[1], Chen Chen[2], Xiaoshuang Liu[1], Bo Wang[1], Ying Sun[1], Maocang Yan[3], Xiaoying Zhang[1*]

[1.] College of Veterinary Medicine, Northwest A & F University, Yangling 712100, China;
[2.] Shaanxi Key Laboratory of Resource Biology, Shaanxi University of Technology, Hanzhong 723000, China;
[3.] Zhejiang Mariculture Research Institute, Wenzhou 325005, China.
E-mail: zhang.xy@nwsuaf.edu.cn

Abstract: The clam *Meretrix meretrix* Linnaeus (*M. meretrix*, Veneridae), is a popular edible shellfish with abundant nutrition and valuable medical properties widely distributed in eastern Asia. As a kind of popular sea food diet, many bioactive components such as peptides, proteins, enzymes, polysaccharide, minerals, essential vitamins, essential amino acids and enzyme inhibitors, have been purified from *M. meretrix*, which are considered to be responsible for its nutritional and medicinal functions including anticancer, antioxidant, antihyperglycemia, antihperlipemia, reduce swelling and detoxification effects. This article reviewed the nutritional constituents, bioactive compounds and pharmacological effects of *M. meretrix* to provide further support and evidence for its medicinal and nutritional use.
[Xie W, Chen C, Liu X, Wang B, Sun Y, Yan M, Zhang X. ***Meretrix Meretrix*: Active Components and Their Bioactivities**. *Life Sci J* 2012; 9(3):756-762] (ISSN:1097-8135). http://www.lifesciencesite.com. 107

Keywords: *Meretrix meretrix (M meretrix)*; clam; nutrition; bioactive components

1. Introduction

Meretrix meretrix Linnaeus (*M. meretrix*, *Meretrix*, Veneridae), commonly known as Asiatic hard clam, is a historically marine food and a valuable source of traditional Chinese medicine (TCM). *M. meretrix* prefers the estuarine and coastal ecosystems and is widely distributed in coastal areas of South and Southeast Asia, including China, Korea, Japan and India (Jayabal, 1986; Ho, 1994). There are a total of 38 species and subspecies in the Genus *Meretrix* including *M. meretrix*, *M. casta*, *M. lamarckiI*, *M. lamarckii*, etc. *M. lurosia* has been considered as a synonym of *M. meretrix* according to the systematization (Pan BP *et al*., 2006).

M. meretrix was documented in the ancient Chinese pharmacopeia *Compendium of material* (the 16th century, by LI Shizhen) which stated *M. meretrix* could diminish inflammation, treat typhoid fever, hangover and relieve pains. Another ancient Chinese medicinal book *Treatise on Fevers* (the 2th century, by ZHANG Zhongjing) stated its special activities of eliminating cyst and detoxification. Many bioactive components such as peptides, proteins, enzyme and enzyme inhibitors have been purified and identified from *M. meretrix* in the recent years, and their functional effects including antihypertensive, hypolipidemic, antineoplastic and antioxidant effects have been proved (Xu *et al*., 1999; Zhao *et al*., 1997; Wei *et al*., 2007 and Huang *et al*., 2005). The clam shells are rich in calcium and have been applied to poultry industry. The calcium oxide derived from *M. meretrix* shells has been demonstrated to be an active biodiesel production catalyst (Viriya-empikul *et al*., 2010). Besides, *M. meretrix* shell can be used for decorative and ornamental purposes.

2. Pharmacological activities

2.1 Antitumor activity

Many antitumor ingredients including polypeptide, polysaccharide and nucleic acid (Table 1) have been purified and functionally confirmed from *M. meretrix*. They exhibit broad antitumor activities in various cancer cell lines of broad organs, and are also in limited *in vivo* trails.

2.2 Antioxidant activity

Proteins and peptides of antioxidant potentials have been confirmed from *M. meretrix*.

Three proteins (P1, 18kD; P2, 28kD and P3, 16kD) isolated from the meat of *M. meretrix* were evaluated for catalase (CAT) activity, superoxide dismutase (SOD) activity and inhibitory effect on lipid peroxidation (LPO) (Xiao *et al*., 2007). P2 exhibited the highest CAT activity (77.0 U/mg), while P3 showed the strongest SOD activity (68.8 U/mg) among the groups. P3 also demonstrated inhibitory effect against lipid peroxidation induced by Fe^{2+}.

After acid protease and trypsase treatments, the *M. meretrix* hydrolyzates exhibited hydroxy radical scavenging activities of 67.75% (Yan *et al.*, 2007) and 94.07% (Qiu *et al*., 2010), respectively. Furthermore, the acid-protease-induced hydrolyzates presented strong superoxide radical scavenging activity (62.79%) (Yan *et al*., 2007).

The antioxidant response of *M. meretrix* has been evaluated by exposing to tributyltin (TBT) of environmentally relevant concentration which could induce oxidative stress (Huang *et al*., 2005). After 2 days' exposure under TBT at the dose of 0.1ng/L, *M. meretrix* expressed approximately 0.2 μmol/min/mg additional glutathione S-transferase (GST) than control group, while the amount of glutathione

peroxidase (GPx) was elevated significantly after exposure for 20 days at the TBT dose of 10 ng/L, suggesting that *M. meretrix* antioxidant response could be enhanced after external challenges.

2.3 Immuno-modulatory activity

After hydrolytes of *M. meretrix* flesh of oral administration to mice at the dose of 20 g/kg for 7 days, the thymus weights of mice increased and the hemolysin antibody activity of mice were enhanced. In a sheep red blood cell (SRBC) induced delayed type hypersensitivity (DTH) model, the hydrolysates could depress DTH, while inhibited the clearance of carbon particles, suggesting that the immunologic function of hydrolysates of *M. meretrix* was alterable in different stages (Yu *et al*., 1991). It was also documented that *M. meretrix* polypeptide could improve mice immunity by promoting the growth of thymus and spleen (Zheng *et al*., 2008).

After polysaccharide of the oral administration isolated from *M. meretrix* to immune system damaged mice induced by cyclophosphamide, a series of immunological indicators, including the phagocytic power, the number of leukocyte, the level of hemolysin antibody, were ameliorated, and DTH reaction was enhanced in mice (Dou *et al*., 1999). *M. meretrix* polypeptide and crude extracts both played as immunosuppressor and immnopotentiator against excessive and inhibitory DTH, respectively (He *et al.*, 1995).

Ethanol extract of *M. meretrix* could enhance the expressions of T- and B-lymphocytes by 18% and 43%, respectively (Zhang *et al.*, 2005).

2.4 Antihyperglycemia and antihperlipemia activities

M. *meretrix* hydrolysate was administrated to diabetic mice and hyperlipidaemia rats for 4 and 8 days at the dose of 10 g/kg for 8 days, respectively. Compared to control groups, the contents of blood sugar decreased by 74.6 mg/dL and by 157.5 mg/dL, respectively. The concentration of triglyceride (TG) and the total cholesterol (TC) in serum of hyperlipaemia rats were reduced by 11.9 mg/dL and 56.1 mg/dL, respectively (Xu *et al*., 1999). Zhang *et al.* (1997) reported that the hydrolysate of *M. meretrix* soft tissue could also reduce the whole blood viscosity in both normal and experimental quail groups and could inhibit the platelet aggregation induced by adenosine diphosphate (ADP) in rabbits.

The polysaccharides extracted from *M. meretrix* also demonstrated antihyperglycemia activity in mesoxyalyurea- induced diabetic rats by remarkably decreasing the level of blood sugar and enhancing stress response on diabetics (Yuan *et al.*, 2007).

3. Chemical and nutritional constituents

M. meretrix is commonly consumed as sea food diet and contains multiple classes of physiological functional ingredients (Table 2) including proteins, polysaccharide, minerals, essential vitamins and essential amino acids (Table 3) (Gopalakrishnan *et al.*, 2009; Yang *et al*., 2007). The concentrations of calcium, magnesium, iron and copper are 175 μg/g, 29 μg/g, 1.75 μg/g and 0.69 μg/g, respectively. *M. meretrix* has high eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) contents of 6.9% and 7.2%, respectively (Yang *et al*., 2007). Taurine, as a kind of organic acid which is essential for cardiovascular function, development and function of skeletal muscle, the retina and the central nervous system, is widely distributed in *M. meretrix* tissues of the high contents of 2.3% and 0.4% from dry and wet *M. meretrix*, respectively (Gong *et al.*, 2003). Vitamin C and Vitamin E were also isolated from wet *M. meretrix* at the concentrations of 5.83μg/mg, 2.6μg/mg, respectively (Gopalakrishnan *et al.*, 2008).

4. Functional proteins, enzymes and enzyme inhibitors

4.1 Ferritin and metallothionein

Ferritin, which occurs in multiple forms in marine animals such as bivalve mollusk, plays an important role for iron storage and metabolism. A full-length ferritin subunit cDNA named MmeFer was cloned and characterized (Wang *et al.*, 2009). The increasing expression of MmeFer mRNA in different developmental stages of *M. meretrix* suggested that ferritin may be involved in shell formation.

Metallothioneins (MT) are cysteine-rich, low- molecular weight and inducible metal-binding proteins with key functions in metal homeostasis and deoxidation, and act as broad protective roles including detoxification of heavy metals, scavenging of free radicals and storing and carrying trace elements. Two MT genes, named *Mm- MT* and *MT*, with a 657bp and a 637bp full- length cDNA both containing an open reading frame of 231bp and encoding a protein of 76 amino acid residues were identified and cloned from *M. meretrix*, respectively (Gao *et al*., 2009; Wang *et al.*, 2010).

4.2 Lectin

Lectins are sugar-binding proteins which possess particular biological properties such as regulating of cell adhesion, glycoprotein synthetization and controlling of protein levels in blood. Kim *et al.* (1990) isolated and purified a carbohydrate-binding protein named MLA-1 from the hemolymph of the shellfish *Meretrix lusoria* (Veneridae), which exhibited hemagglutination and carbohydrate specificity. Zhao *et al*. (1992) isolated a specific sialic acid binding lectin (MML) from *M. meretrix*, which can widely agglutinate various kinds

Table 1. Antitumor components isolated from *M. meretrix*

Ingredient	Name	MW (Da)	Antitumor activities	Referen -ces
Polypeptide	Mercenene	≤ 10000	Strongly inhibit Sarcoma 180 (S180) and Krebs 2-breast carcinoma, Hale cell lines.	Schmeer *et al.* (1964, 1979)
	Mer2	N/A	Inhibit the proliferation of HepG2, Hela, QBC939, SPC-A-1 cell lines at dose of 80 μg /ml with inhibitory rate of 78.3%, 72.9%, 67.6% and 53.2%, respectively.	Fan *et al.* (2009)
	MGP_{0501}	15878	Inhibit the proliferation of K562, A549, HO8910 cell lines with IC_{50} of 32.03 μg/ml, 20.34 μg/ml and 29.13μg/ml respectively.	Wu *et al.* (2006)
	MGP_{0405}	9655	Inhibit the proliferation of B16, KB, A549, Hela, K562, BGC, HO8910 and SMMC-7721 cell lines with IC_{50} of 178μg/ml, 132μg/ml, 178μg/ml, 181μg/ml, 264μg/ml, 202μg/ml, 468μg/ml and 204μg/ml, respectively.	Zhang *et al.* (2009)
	MML	40000	Inhibit the growth of BEL-7402 which was transplanted into nude mice *in vivo* with IC_{50} of 52.2μg/mL.	Zhang *et al.* (2009)
	M2	18000	Inhibit the proliferation of BGC-823 cells and destroy their skeletal structures.	Liu *et al.* (2004)
Polysaccharide	N/A	N/A	Inhibit the growth of S180 *in vivo* (inhibitive rate of 43.64% at the dose of 100mg/kg), prolong the survival period of mice with EAC ascites carcinoma and hepatic carcinoma.	Wu *et al.* (2006)
Nucleic acid	N/A	N/A	Inhibit the proliferation of S180 and HepA with inhibitory rate of 43%-61% and 37%, respectively.	Zhang *et al.* (1990)

Note: N/A: data not available

of RBC agglutination activity. The Ca^{2+} dependent lectin is sensitive to high temperature (over 40 ℃) and to the extreme pH (over 8.5 or below 5.0). The MML was 59kDa and naturally consisted of two kinds of subunits of MML (WM 29 kDa, 30kDa) connected by-S-S- . The lectin was also reported to contain 5 percentage of sugar and have the ability of inhibiting or even killing cancer cells - human malignant lymphoblast (Raji cells).

4.3 Heat shock protein

MmeHsc71, a heat shock protein (HSP) (71.43 kDa), was found in *M. meretrix* and determined to be a member of the hsp70 family (Yue *et al.*, 2011). Based on the comparison of the spatial and temporal expression of MmeHsc71 in mRNA level between normal clams and *vibrio parahaemolyticus*- infected clams, MmeHsc71 mRNA could be found in all tested tissues including foot, hepatopancreas, mantle and gill. Moreover, the expression of MmeHsc71 mRNA in hepatopancreas of *vibrio parahaemolyticus*- infected clams was 2- fold of that of normal clams. This result can be further confirmed in a quantitative immunofluorescence analysis; the protein level of MmeHsc71 in *vibrio parahaemolyticus*- infected clams was higher than that of control group at 24 h post-infection, indicating that MmeHse71 may play a crucial role in mediating the immune responses of *M. meretrix* to bacterial challenges.

4.4 Adenosine diphosphate ribosylating protein

Adenosine diphosphate (ADP) - ribosylation plays a significant role in the posttranslational modification by transferring to its acceptor molecules mediated by the ADP-ribose moiety of β-NAD. Nakano *et al.* (2006) found a DNA ADP-ribosylation protein named CARP-1 in the hard clam *M. lamarckii*. After purification methods of ammonium sulfate fractionation, carboxymethyl-cellulose chromatography and CM52 column, a mass of molecular weight of 20 kDa was highly enriched. In addition, the DNA of ADP-ribosylating protein was purified and its cDNA was cloned which encodes 182 amino acids.

4.5 Lysozyme

Lysozymes have strong antimicrobial activity by damaging bacterial cell wall.

Lysozyme, named Mmelys, was cloned and sequenced from *M. meretrix*, and it consisted of a 15 amino acid signal peptide and an 131 amino acid mature protein. Mmelys presented high mRNA level and protein level in gill and hepatopancreas. Mmelys showed regressive inhibitory effect against *P. aeruginosa* and *M. luteus* at the purified enzyme doses of 375μg /mL and 250 μg /mL, respectively (Yue *et al.*, 2010).

4.6 Cathepsin B

Cathepsin B, belongs to the papain super family, is a key proteolytic in the nutrient metabolism of *M. meretrix*. It has been considered that cathepsin B can degrade β-amyloid precursor protein into harmless fragments, and can also possess endopeptidease, dipetidylcarboxy peptidase activities. The full length of cathepsin B (MmeCB) cDNA was cloned and it was constituted of 1647 bp, with an open reading frame of 1014 bp encoding a preproenzyme of 337 residues with Cys-114, His-282 and Asn-302 composing cathepsin B activity center (Wang *et al.*, 2008). No MmeCB mRNA was found in trochophore stage. In the later stages, detectable signals were found, suggesting that MmeCB may play a role in nutrient digestion. Further analysis showed that MmeCB may be also associated with other pathways of nutrient metabolism in larval epidermis. A recombinant fusion protein GST-MmeCB of high level was obtained from *Escherichia coli* and the recombinant MmeCB can degrade the selective substrate. The kinetic parameters of rMmeCB were calculated as follows: K_m, V_{max}, and k_{cat} were 6.11uM, 0.0174uM min^{-1} and 277.57s^{-1}, respectively. Further analysis showed that cathepsin B was probably involved in the nutrient digestion of *M. meretrix* (Yao *et al.*, 2010).

4.7Angiotensin converting enzyme inhibitor

The presence of Angiotensin converting enzyme (ACE) shows great importance in the regulation of blood pressure, which catalyzes the conversion of angiotensin I into activated angiotensin II. Angiotensin II has the properties of inducing aldosterone release; resulting in Na^+ entering cell, blood pressure raise. Inhibition of ACE may reduce the formation of angiotensin II and then release blood pressure. ACE-inhibitory peptides were derived from the meat of *Meretrix lusoria* hydrolyzed by Protamex (PX) of IC_{50} of 0.036mg/mL. Two peptides (E1, E2) purified by Sephadex G-25 column and RP-HPLC, E2, containing two amino acids residues (Tyr-Asn), showed higher inhibitory effect of IC_{50} of 51 μM (0.015 mg/ml) assayed by using a modified spectrophotometric method (Tsai *et al*., 2008).

4.8 Glutathione peroxidase

Glutathione peroxidase (GSH-Px), a kind of peroxidase, can protect the organism from oxidative damage by reducing lipid hydroperoxides to their corresponding alcohols and reducing free hydrogen peroxide to water. Wang *et al.* (2011) cloned glutathione peroxidase MmeGPx genes, which included two introns (723bp and 238bp) with an open reading frame of 711bp coding a protein of 76 amino acids.

4.9 Strombine dehydrogenase (SDH)

Lee *et al.* (2011) isolated and purified SDH from foot of *M. meretrix* by adopting ammonium sulfate precipitation, passing through sephacryl S-100 column and hydroxyapatite chromatography, and some other chromatographic programs. SDH is heat labile, and is of high enzyme activity under the optimal pH and temperature of 7.4–7.6 and 45℃–46℃, respectively. L-Alanine, glycine, and pyruvate are its preferred substrates.

Furthermore, a series of enzymes had been found in *M. meretrix*, including lactic dehydrogenase (Lee *et al.*, 2011), antioxidase (Wang *et al*., 2010), adenosine deaminase (Aikawa *et al*., 1966), alkaline phosphatase (Aikawa *et al.*, 1966), phosphohydrolase etc. (Umemori *et al*., 1967).

5. Prospective

Estuarine and coastal ecosystems provide productive aquatic resources since the unique environment where seawater meets and mixes with fresh water. As well, it is also good environment for the growth of bacteria and sediments, suggesting the bivalves need to develop their defense systems against potential pathogens and microorganisms which may induce them to synthetize unique chemical components of potential medicinal values.

Edible bivalves such as *M. meretrix* are in growing demand due to their abundant nutrition and valuable medical properties. *M. meretrix* was also elucidated as an excellent source for proteins, polysaccharide, minerals, essential vitamins and essential amino acids (Gopalakrishnan *et al.*, 2009; Yang *et al.*, 2007).

Many bioactive substances have been found in *M. meretrix*. However, related studies are still inadequate. Efforts should be made to further explore their bioactivities and medicinal functions as well as their mechanisms. TCM could provide a useful reference for this kind of investigations.

Table 2. Mainly functional ingredients of *M. meretrix* (wet weight)

Constitution	Content (%)	References
Crude protein	10.5-15.54	Yang *et al.* (2007); Li *et al.* (2010)
Crude fat	1.07-6.78	Zhang *et al.* (2006); Li *et al.* (2010)
Carbohy-drate	4.14-8.3	Li *et al.*(2010); Kang *et al.* (2008)
Moisture	76.39-80.2	Yang *et al.* (2007); Li *et al.* (2010)
Ash	12.8-22.4	Kang *et al.* (2008); Zhang *et al.* (2006)

Table 3. Essential amino acids in *M. meretrix* (wet weight)

Amino acid	Content (mg/g)
Isoleucine	36.4
Leucine	52.1
Threonine	26.9
Valine	26.5
Tyrosine	32.1
Tryptophan	7.6
Lysine	42.2
Methionine	26.7

Acknowledgments

This work was supported by Science & Technology Planning Program (No. S20100016, 2011-2013) of Wenzhou city and "Overseas Teacher" project (No.MS2011XBNL057) of the Ministry of Education and State Administration of Foreign Experts Affairs, China.

Corresponding Author:

Prof. Dr. Xiao-Ying Zhang
College of Veterinary Medicine
Northwest A & F University (North Campus)
Yangling, Shaanxi Province, 712100, China
Tel. & Fax: +86 29 87091239
E-mail: zhang.xy@nwsuaf.edu.cn

References

1. Aikawa T. Adenosine aminohydrolase from the clam, Meretrix meretrix Lusoria (Gmelin). Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology, 1966;17 (1):271-84.
2. Dou CG, Huang F, Huang LS, Bu WJ. An experimental study on the effects of Meretrix meretrix polysaccharide on antineoplastic and immunoregulation. Chinese Journal of Marine Drugs (in Chinese) 1999;70 (2):15-9.
3. Fischer-Piette E. Revision des vivanuts de Meretrix s.s. du museum national of histoirenaturelle. Journal of Conchyliol 1941;84 (21):315-44.
4. Gao XG, He CB, Li YF, Wang J. Analysis on Cloning and sequence Characteristics of Metallothionein Gene in Hard Clam Meretrix meretrix. Chinese Journal of Fisheries (in Chinese) 2009;22 (4): 8-11.
5. Gong LF, Huang WS, Xie XL, Zheng ZF, Hu DH. Extraction of taurine from Meretrix meretrix. Fine Chemicals 2003;20 (7):393-95.
6. Gopalakrishnan S, Vijayavel K Nutritional composition of three estuarine bivalve mussels, perna viridis, donax cuneatus and meretrix meretrix. International Journal of food science and nutrition 2009;60 (6):458-63.
7. He YJ, Wu Q, Zhu RF. Immunomodulating effects of the extract from clam Meretrix meretrix on delayed hypersensitivity in mice. Chinese Journal of Marine Drugs (in Chinese) 1995;55(3): 20-1.
8. Ho JS, Zheng GX. Ostrincola koe (Copepoda, Myicolidae) and mass mortality of cultured hard clam (Meretrix meretrix) in China. Hydrobiologia 1994;284 (2):169-73.
9. Huang XP, Liu L, 1996. Enzymatic hydrolysis research on meat of Meretrix meretrix. Food science (in Chinese);17(9):21-4.
10. Huang ZH, Chen YX, Zhao Y, Zuo ZH, Chen M. Antioxidant responses in Meretrix meretrix exposed to environmentally relevant doses of tributyltin. Environmental Toxicology and Pharmacology 2005;20 (1):107-11.
11. Jayabal, R., Kalyani, M., 1986. Reproductive cycles of some bivalves from Vellar Estuary, east coast of India. Indian Journal of Marine Sciences, 15(1), 59-60.
12. Kang JH, Zheng GX, Fan CH. Analysis of Components in Meretrix meretrix Peptides. Journal of Xiamen University (in Chinese) 2008;47(sup 2):135-7.
13. Kim JH, Chung SR. Lectin from Marine Shells (IX): Purification and Carbohydrates Specificities of a Lectin, MLA-1, from the Hemolymph of Meretrix lusoria. Korean Biochemical Journal 1990;23 (3):328-34.

14. Lee AC, Lee KT, Pan LY. Purification and kinetic characteristics of strombine dehydrogenase from the foot muscle of the hard clam (Meretrix lusoria). Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology 2011;158 (1):38-45.
15. Leng B, Liu XD, Chen QX. Inhibitory effects of anticancer peptide from Mercenaria on the BGC-823cells and several enzymes. FEBS Letters 2005;579 (5):1187-90.
16. Liu XD, Qiu L. Studies on the Physiological Activity of a Natural Peptide from Clam
17. (Meretrix meretrix Linnaeus). Journal of Xia men University (Natural Science) (in Chinese) 2004;43 (4):432-35.
18. Li XY, Dong ZG, Yan BL. Analysis and Evaluation of Nutritional Components in Cyclinasinensis and Meretrix meretrix. Food Science (in Chinese) 2010;31(23):366-70.
19. Ning X, Zhao J, Zhang Y. A novel anti-tumor protein extracted from Meretrix meretrix Linnaeus induces cell death by increasing cell permeability and inhibiting tubulin polymerization. International Journal of Oncology 2009;35 (4):805-12.
20. Nakano T, Matsushima-Hibiya Y, Yamamoto M, Wakabayashi K. Purification and molecular cloning of a DNA ADP-ribosylating protein, CAPP-1, from the edible clam Meretrix lamarckii. Proceedings of the National Academy of Sciences 2006;103 (37):13652-7.
21. Nazeer RA, DivyaPrabha KR, Sampath Kumar NS. Isolation of antioxidant peptides from clam Meretrix casta (Chemnitz). Journal of Food Science and Technology 2011 Online Available at: http://www.springerlink.com/content/457q24362r33t871/. Accessed on 10 June 2011.
22. Pan BP, Wu Q, Zhang SP, Song LS. Molecular phylogeny of meretrix (Mollusca, Bivalvia) based on 16S rRNA genes and ITS1 sequences. Oceanologia et Limnologia Sinica 2006;37(4):343-7.
23. Qiu CJ, Yao XG, Zhao PP. Separation and purification the Minor Peptides from the Meretrix Linnaeu Protein Hydrolysates and the Investigation of the Biochemical Properties. Food Research and Development 2010;31(5):4-6.
24. Schmeer MR. Growth-Inhibiting Agents from Mercenaria Extracts: Chemical and Biological Properties. Science 1964;144 (3617):413-4.
25. Schmeer MR, Horton D, Tanimura A. Mercenene, a tumor inhibitor from Mercenaria: purification and characterization studies. Life Science 1966;5 (13):1169-78.
26. Tsai JS, Chen JL, Pan BS. ACE-inhibitory peptides identified from the muscle protein hydrolysate of hard clam (Meretrix lusoria). Process Biochemistry 2008;43 (7):743–7.
27. Viriya-empikul N, Krasae P, Puttasawat B, Yoosuk B, Chollacoop N, Faungnawakij K. Waste shells of mollusk and egg as biodiesel production catalysts. Bioresource Technology 2010;101(10): 3765-7.
28. Wang C, Huan P. Molecular characterization of a glutathione peroxidase gene and its expression in the selected Vibrio resistant population of the clam Meretrix meretrix. Fish and Shellfish Immunology 2011;30 (6):1294-302.
29. Wang Q, Wang X, Wang X. Analysis of metallotionein expression and antioxidant enzyme activities in Meretrix meretrix larvae under sublethal cadmium exposure. Aquatic Toxicology 2010;100(4): 321-8.
30. Wang XM, Liu BZ, Wang GD, Tang BJ, Xiang JH. Molecular cloning and functional analysis of cathepsin B in nutrient metabolism during larval development in Meretrix meretrix. Aquaculture 2008;282 (1-4): 41-6.
31. Wang X, Liu B, Xiang J. Cloning, characterization and expression of ferritin subunit from clam Meretrix meretrix in different larval stages. Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology 2009;154 (1):12-6.
32. Wei N, Lin XK, Niu RL, Li HY. Overview on anticancer agents from Meretrix meretrix. Food and Drug (in Chinese) 2007;9 (11):63-5.
33. Wu LJ, Zhang B, Huang CH, Zhu XC. The antitumor activity of Glycopeptide (MGP0501) from Meretrix meretrix in Vitro. Pharmaceutical Biotechnology 2006;13(4):260-4.
34. Wu TH, Yang RL, Xie LP. Inhibition of cell growth and induction of Gl-phase cell cycle arrest in Hepatoma cells by steroid extract from Meretrix meretrix. Cancer Letters 2006;232(2):199-205.
35. Xiao X, Chen X. Isolation and autoxidation of bioactive proteins from Meretrix meretrix. Chinese Journal of Marine Drugs (in Chinese) 2007;26 (6):24-27.
36. Xu XL, Li TM, Zhang CR. Study on Antihyperglycemia and AntihyperLipenmia

Action of Hydrolysate of Meretrix meretrix Linnaeus. Chinese Journal of Biochemical Pharmaceutics (in Chinese) 1999;20 (6):298-9.
37. Yang J, Tao NP, Wang XC. Nutritional composition of Meretrix meretrix and effect on Flavor. Food and Nutrition in China (in Chinese) 2007; 5 (1):43-45.
38. Yan YX, Su GJ, Li XM. Study on antioxidative bioactive peptide of Meretrix meretrix protein. Science and Technology of Food Industry 2007;12 (28):121-123.
39. Yao XL, Zhang JQ, Sun JS. Recombinant expression, characterization and expressional analysis of clam Meretrix meretrix cathepsin B, an enzyme involved in nutrient digestion. Molecular Biology Reports 2011;38 (3):1861Yoko U. Ribonucleotide phosphohydrolases in the clam, Meretrix meretrix lusoria (Gmelin). Comparative Biochemistry and Physiology 1967;20 (2):635–39.
40. Yoko UA. An alkalinephosphatase in the clam Meretrix meretrix lusoria (Gmelin), with affinities for nucleotides. Comparative Biochemistry and Physiology Part B: Comparative Biochemistry, 1971;40 (2):347–58.
41. Yuan Q, Yuan H. Effect of Meretrix polysaccharides on blood sugar regulation and stress response in the experimental diabetic rats. Chinese Journal of Modern Applied Pharmacy (in Chinese) 2007;24 (2):113-4.
42. Yue X, Liu B, Sun L. Cloning and characterization of a hsp70 gene from Asiatic hard clam Meretrix meretrix which is involved in the immune response against bacterial infection. Fish and Shellfish Immunology 2011;30 (3):791-9.
43. Yue X, Liu B, Xue Q. An i-type lysozyme from the Asiatic hard clam Meretrix meretrix potentially functioning in host immunity. Fish and Shellfish Immunology 2011;30 (2):550-8.
44. Yu ZL, Dou CG., Jiang WJ. Effect of hyrolysate of Meretrix meretrix flesh on immunologic function in mice. Chinese Journal of Marine Drugs (in Chinese) 1991; 40 (4):15-7.
45. Zhang B, Wu WT, Wu LJ. Studies on Stability and Anticancer Activities of Meretrix meretrix Glycopeptide MGP0405. Pharmaceutical Biotechnology 2006;13 (1):24-7.
46. Zhang GQ, Yu ZL, Zhao HC. A study on hypolipemic effect of hydrolysate of Meretrix meretrix soft tissue in quail.Chinese Journal of Marine Drugs (in Chinese) 1997;16 (2):21-4.
47. Zhang J, Kang JH, Liu FJ, Fan CC, Li HL. Effect of the polypeptides from Meretrix meretrix Linnaeus on proliferation of cervical cancer Hela Cells. Journal of Xiamen University (in Chinese) 2009;48(5);729-32.
48. Zhang LX, Fan X, Han LJ. Antitumor and immune regulation activities of the extracts of same Chinese marine invertebrates. Chinese Journal of Oceanology and limnology 2005;23 (1):110-7.
49. Zhang XJ, Xing YP. Studies on anti-cancer activity of Meretrix meretrix nucleic acid.Chinese Journal of Oceanology and Limnology 1990;21(1):88-91.
50. Zhao GD, Su B. The preliminary studies on the Lectin from Sea Clam (Meretrix meretrix). Journal of Zhong Shan University (Natural Science) (in Chinese) 1992;31 (3):66-74.
51. Zheng GX, Fan CC, Kang JH, Leng B. Inhibition effect of polypeptide from Meretrix meretrix on liver cancer cells SMMC-7721 and its physiological studies on mice. Journal of Xiamen University (in Chinese) 2008;47 (sup 2): 138-14.