

**IDENTIFICATION AND CHARACTERIZATION  
OF PROTEINS FROM SABAH EDIBLE  
SEAWEEDS BY USING PROTEOMICS  
APPROACH**

**FISAL BIN AHMAD**

**THESIS SUBMITTED IN PARTIAL  
FULFILLMENT FOR THE DEGREE OF DOCTOR  
OF PHILOSOPHY**

**PERPUSTAKAAN  
UNIVERSITI MALAYSIA SABAH**

**FACULTY OF FOOD SCIENCE AND NUTRITION  
UNIVERSITI MALAYSIA SABAH  
2016**



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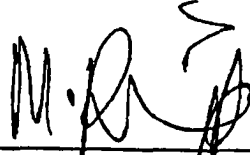
  
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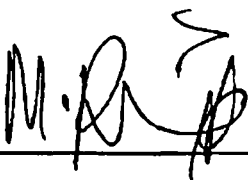
NAME : **FISAL AHMAD**  
Matrik No. : **PN 20119010**  
TITLE : **IDENTIFICATION AND CHARACTERIZATION OF  
PROTEINS FROM SABAH EDIBLE SEAWEEDS BY  
USING PROTEOMICS APPROACH**  
DEGREE : **DOCTOR OF PHILOSOPHY**  
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### CERTIFIED BY

**1. CHAIRMAN**

Associate Prof. Dr. Mohd Rosni Sulaiman

Signature



---

**2. COMMITTEE MEMBER 1**

Associate Prof. Dr Chye Fook Yee



---

**3. COMMITTEE MEMBER 2**

Associate Prof. Dr Patricia Matanjun



---

**4. COMMITTEE MEMBER 3**

Associate Prof. Dr Azwan Awang

---

## ACKNOWLEDGEMENTS

In the name of ALLAH, Most Gracious, Most Merciful. Alhamdulillah, the will of Almighty Allah s.w.t has given me the ability to finish my project and finally, this thesis is completed.

I would like to express my heartfelt appreciation to my supervisor Assoc. Prof. Dr. Mohd Rosni Sulaiman for his valuable time, guidance, advice and critics in fulfilling the study. Special thanks to my committee members Assoc. Prof. Dr. Azwan Awang, Assoc. Prof. Dr. Chye Fook Yee and Assoc. Prof. Dr. Patricia Matanjun for their guidance, advice and encouragement over these years.

Many thanks to Dr. Ahmad Nazri Ismail and the Doping Control Centre, USM for the knowledge and skills I gained while working with them. They provided useful discussions on both my research area and other branches of Bioinformatics.

I also would like to thank my mom and all my family members who have been so cooperative and understanding, for their love, support and motivation that give me strength and passion to work hard to fulfil my goal and complete this thesis.

Last but not least, my heartfelt thanks to Assoc. Prof. Dr. Aznawati, Mr. Mansor, Dr. Hasmadi, Dr. Mohd Khalizan, all lab members, my faculty mates, my friends and colleagues for their cooperation, technical assistance and helping hand. Thank you for their endless love and always be by my side.

Fisal bin Ahmad  
10 July 2016

## ABSTRACT

The present study was carried out to examine the proteome profile of selected seaweed species from Sabah waters to explore their nutritional properties. Moisture content was a major component in seaweed followed by carbohydrate, mineral, and protein. The results showed significant differences ( $p < 0.05$ ) in proximate compositions and total phenolic contents among several species of red, green and brown seaweeds. Studies showed that red seaweed higher in carbohydrate (63 to 74 % dry weight) and protein (6 to 15 % dry weight) content. Brown seaweed higher in mineral (22 to 45 % dry weight) and fibre (21 to 45 % dry weight) content. Meanwhile, green seaweed higher in total phenolic content (48 to 52 mg PGE/g dry weight sample). Using *Caulerpa lentillifera*, four different protocols for protein extraction were evaluated, namely: (i) no protein precipitation with fractionation; (ii) Trichloroacetic acid (TCA)-acetone precipitation; (iii) TCA-acetone precipitation with fractionation; and (iv) Phenol extraction methanol-ammonium acetate precipitation. Overall, the phenol extraction method gave a higher protein yield and some protein spots resolved with a satisfactory 2D-PAGE image quality than the other methods. Thus this method was used to extract total soluble protein from all 15 seaweed samples. There was a strong positive correlation between crude protein and total soluble protein concentration ( $r = 0.952$ ;  $p = 0.007$ ) in these fifteen varieties of seaweed. A distinctive protein pattern was observed in the SDS-PAGE gels between three different seaweed classes of green, red and brown colours. Using this method of extraction, it managed to get 2D-PAGE proteome map for three seaweeds species, namely *Caulerpa lentillifera*, *Kappaphycus alvarezii* and *Sargassum polycystum*. The image analysis of 2D-PAGE was performed with Progenesis SameSpots v 4.5 and four sets of comparison of the 2D-PAGE gel image were done, Set 1: *Caulerpa lentillifera* fronds-CLB vs *Caulerpa lentillifera* stolon-CLT; Set 2: *Kappaphycus alvarezii* small branches-KAK vs *Kappaphycus alvarezii* big branches-KAB; Set 3: *Sargassum polycystum* vacuoles-SPB vs *Sargassum polycystum* leaves-SPD vs *Sargassum polycystum* stolon-SPT; and Set 4: *Caulerpa lentillifera*-CLS vs *Kappaphycus alvarezii*-KAS vs *Sargassum polycystum*-SPS to detect differentially expressed protein spot. Results of image analysis revealed 77 differentially expressed proteins for experiment set of CLB vs. CLT, 98 differentially expressed proteins for experiment set of KAK vs. KAB, 93 differentially expressed proteins for experiment set of SPB vs. SPD vs. SPT and 148 differentially expressed proteins for experiment set of CLS vs. KAS vs. SPS. Only 20 differentially expressed proteins from all four sets of experiments have been successfully identified and characterized by using nano-LC-MS/MS (Orbitrap) and Bioinformatics Software PEAKS Studio 7. Most of the identified proteins were a non-enzyme protein such as light-harvesting phycobiliprotein, light-harvesting complex, histone, and elongation factor. The enzyme proteins identified were ribulose biphosphate carboxylase and glyceraldehyde-3-phosphate dehydrogenase. Regarding health benefits, the potential evaluation of the peptide profile results showed that protein extracts from the three seaweeds species contain peptide sequences with a variety of beneficial health effects. From among 44 types of biological activity characteristics of peptides, as listed in the BIOPEP database, motifs with the Dipeptidyl Peptidase IV inhibitors and ACE inhibitory activity occur most frequently in all protein sequences from the seaweed samples. Others bioactive peptide present, such as antioxidant, stimulating, regulating, anti-amnesic, antithrombotic and many other activities. Therefore, this protein raw material, which currently remains a relatively untapped reservoir, has the potential to act as a resource for the generation of bioactive peptides with potential health-promoting and disease-preventing properties. Hopefully, these findings will contribute towards seaweed protein utilization as alternative sources of peptide-based nutraceuticals for human health promotion.

## ABSTRAK

### **PENGENALPASTIAN DAN PENCIRIAN PROTEIN DARIPADA RUMPAILAUT SABAH DENGAN MENGGUNAKAN KAEDAH PROTEOMIK**

Kajian yang telah dijalankan ini adalah untuk menilai profil protein pada spesies rumpailaut yang terpilih daripada perairan Sabah yang bertujuan untuk meneroka serta melihat ciri-ciri khasiat yang ada. Kandungan kelembapan merupakan komponen utama dalam rumpailaut diikuti oleh karbohidrat, mineral dan protein. Keputusan kajian menunjukkan perbezaan yang bererti ( $p < 0.05$ ) pada analisis proksimat dan jumlah kandungan fenolik di antara beberapa spesies rumpailaut merah, hijau dan perang. Kajian mendapati bahawa rumpailaut merah mengandungi karbohidrat (63% hingga 47% berat kering) dan kandungan protein (6% hingga 15% berat kering) yang tertinggi. Rumpailaut perang mengandungi mineral (22% hingga 45% berat kering) dan serat (21% hingga 45% berat kering) yang tertinggi. Manakala rumpailaut hijau mengandungi jumlah kandungan fenol yang tertinggi (48 hingga 52 mg PGE/g berat kering sampel). Menggunakan *Caulerpa lentillifera*, empat kaedah pengekstrakan protein yang berbeza telah dikaji iaitu: (i) pembahagian protein tanpa pemendakan; (ii) asid trikloroasetik (TCA)-pemendakan aseton; (iii) Pemendakan asid trikloroasetik (TCA) dengan pembahagian; dan (iv) pengekstrakan fenol-pemendakan methanol-amonium asetat. Secara keseluruhannya, pengekstrakan fenol memberikan hasil protein yang tinggi dan bilangan tompok protein yang terpisah serta gambaran 2D-PAGE yang sangat memuaskan berbanding kaedah lainnya. Oleh yang demikian kaedah ini digunakan untuk mengekstrak jumlah kandungan protein larut pada kesemua 15 sampel rumpailaut. Keputusan juga menunjukkan korelasi positif yang kuat di antara nilai protein kasar dengan kepekatan jumlah protein larut ( $r=0.952$ ;  $p=0.007$ ) pada limabelas varieti rumpailaut tersebut. Corak protein yang berbeza juga ditunjukkan pada gel SDS-PAGE diantara spesies rumpailaut hijau, merah dan perang. Menggunakan kaedah pengekstrakan yang sama, ianya telah menghasilkan peta protein 2D-PAGE untuk tiga spesies rumpailaut iaitu, *Caulerpa lentillifera*, *Kappaphycus alvarezii* var. aring-aring dan *Sargassum polycystum*. Analisis gambar 2D-PAGE telah dibuat menggunakan Progenesis SameSpots v 4.5 dan empat set kajian perbandingan gel 2D-PAGE telah dijalankan iaitu, Set 1: *Caulerpa lentillifera* 'fronds'-CLB dengan *Caulerpa lentillifera* 'stolon'-CLT; Set 2: *Kappaphycus alvarezii* cabang halus-KAK dengan *Kappaphycus alvarezii* cabang besar-KAB; Set 3: *Sargassum polycystum* vakul-SPB dengan *Sargassum polycystum* daun-SPD dengan *Sargassum polycystum* 'stolon'-SPT and Set 4: *Caulerpa lentillifera*-CLS dengan *Kappaphycus alvarezii*-KAS dengan *Sargassum polycystum*-SPS bagi mencari tompok protein yang menunjukkan perbezaan. Keputusan analisis gambar mendapati 77 tompok protein yang berbeza pada set CLB dengan CLT, 98 tompok protein yang berbeza pada set KAK dengan KAB, 93 tompok protein yang berbeza pada set SPB dengan SPD dengan SPT and 148 tompok protein yang berbeza pada set CLS dengan KAS dengan SPS. Hanya 20 tompok protein yang berbeza telah di kenalpasti dan pencirian dilakukan dengan jayanya menggunakan nano LC-MS/MS (Orbitrap) dan perisian bioinformatik PEAKS studio 7. Kebanyakan protein yang dikenalpasti adalah bukan enzim seperti cahaya-tuai pikobiliprotein, kompleks cahaya-tuai, histona dan faktor pemanjangan. Protein enzim yang dikenalpasti adalah seperti ribulosa bifosfat karboksilase dan gliseroldihida-3-fosfat dihidrogenase. Merujuk kepada kebaikan kesihatan, penilaian potensi mendapati ekstrak protein daripada ketiga-tiga spesies rumpailaut mengandungi urutan rantaian peptida yang mempunyai pelbagai khasiat kesihatan. Daripada 44 jenis ciri aktiviti biologi yang terdapat pada rantaian peptida, seperti yang tersenarai pada pengkalan data BIOPEP, motif dengan ciri aktiviti perencat 'Dipeptidyl Peptidase-IV' dan aktiviti perencatan ACE hadir pada kekerapan yang tertinggi tinggi pada semua urutan rantaian protein pada ketiga-tiga rumpailaut. Peptida

*bioaktif lain yang hadir adalah seperti, antioksidan, rangsangan, pengaturan, anti-amnestik, antithrombotik dan lain-lain lagi. Oleh itu, sumber protein ini, yang mana ianya masih lagi belum dibangunkan, mempunyai potensi yang baik untuk menjadi sumber penghasilan peptida bioaktif dengan ciri-ciri kebaikan kesihatan dan juga menjadi penghalang kepada penyakit. Adalah diharapkan dengan dapatan kajian ini dapat menyumbang kepada penggunaan protein daripada rumpai laut sebagai sumber alternatif untuk bekalan bahan asas nutraseutikal peptida untuk penjagaan kesihatan manusia.*





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## LIST OF ABBREVIATION

%	–	Percentage
°C	–	Degree celcius
µg/g	–	Microgram per gram
µg/L	–	microgram perlitre
1D	–	One dimension
2D	–	Two dimension
AcDP	–	Acetone dried powder
ACE	–	Angiotensin-converting enzyme
ACN	–	Acetonitrile
ANOVA	–	Analysis of variance
APS	–	Ammonium persulfate
BLAST	–	Basic Local Alignment Search Tool
BSA	–	Bovine serum albumin
CBB	–	Commase brilliant blue
CHAPS	–	Chloromidopropyldimethylammonio-1-propane sulfonate
CID	–	Collision-induced dissociation
CuSO <sub>4</sub>	–	Copper (II) sulfata
DNA	–	Deoxyribonucleic acid
DTT	–	Dithiothreitol
ECD	–	Electron capture dissociation
ESI	–	Electrospray ionization
<i>et al.,</i>	–	and all
ETD	–	Electron transfer dissociation
FAO	–	Food and agricultural organization
FDR	–	False discovery rates
g	–	Gram
HCl	–	Hydrochloric acid
HPLC	–	High performance liquid chromatography
IEF	–	Isoelectrofocusing



## REFERENCES

- Abhilash, M. 2009. Applications of Proteomics. *The Internet Journal of Genomics and Proteomics*, **4**(1): 1-4.
- Abrantes, J. L., Barbosa, J., Cavalcanti, D., Pereira, R. C., Fontes, C. F. L., Teixeira, V. L., Moreno Souza, T.L., and Paixao, I.C. 2010. The effects of the diterpenes isolated from the Brazilian brown algae *Dictyota pfaffii* and *Dictyota menstrualis* against the herpes simplex type-1 replicative cycle. *Planta Medica*, **76**(1): 339-344.
- Agrawal, G.K., and Rakwal, R. 2006. Rice proteomics: a cornerstone for cereal food crop proteomes. *Mass Spectrometry Reviews*, **25**(1):1-5.
- Aguilera-Morales, M., Casas-Valdez, M., Carrillo- Dominguez, S., Gonzalez-Acosta, B. and Perez-Gil, F. 2005. Chemical composition and microbiological assays of marine algae *Enteromorpha* ssp. as potential food source. *Journal of Food Composition and Analysis*, **18**(1): 79-88.
- Ahmad, F., Sulaiman M.R., Saimon, W., Chye, F.Y. and Matanjun, P. 2012. Proximate compositions and total phenolic contents of selected edible seaweed from Semporna, Sabah, Malaysia. *Borneo Science Journal*, **31**(1): 85-96.
- Ahn, G. N., Kim, K. N., Cha, S. H., Song, C. B., Lee, J. H., Heo, M. S., Yeo, I.K., Lee, N.H., Jee, Y.H., Kim, J.S., Heu, M.S., and Jeon, Y.J. 2007. Antioxidant activities of phlorotannins purified from *Ecklonia cava* on free radical scavenging using ESR and H<sub>2</sub>O<sub>2</sub>-mediated DNA damage. *Journal of European Food Research and Technology*, **226**(1): 71-79.
- Ahn, M. J., Yoon, K. D., Min, S. Y., Lee, J. S., Kim, J. H., Kim, T. G., Kim, T.G., Kim, S.H., Kim, N.G., Huh, H., and Kim, J. 2004. Inhibition of HIV-1 reverse transcriptase and protease by phlorotannins from the brown alga *Ecklonia cava*. *Biological and Pharmaceutical Bulletin*, **27**(1): 544-547.
- Airanthi, M. K. W. A., Hosokawa, M., and Miyashita, K. 2011. Comparative antioxidant activity of edible Japanese brown seaweeds. *Journal of Food Science*, **76**: 104-111.
- Alekseyenko, T.V., Zhanayeva, S.Y.A., Venediktova, A.A., Zvyagintseva, T.N., Kuznetsova, T.A., Besednova, N.N., and Korolenko, T.A. 2007. Antitumor and antimetastatic activity of fucoidan, asulfated polysaccharide isolated from the Okhotsk Sea *Fucus evanescens* brown alga. *Bulletin of Experimental Biology and Medicine*, **143**(1): 730-732.

- Allen, V.G., Pond, K.R., Saker, K.E., Fontenot, J.P., Baglev, C.P., Ivy, R.L., Evans, R.R., Brown, C.P., Miller, M.F., Montgomery, J.L., Dettle, T.M., and Wester, D.B. 2001. Tasco-Forage: III. Influence of a seaweed extract on performance, monocyte immune cell response, and carcass characteristics in feedlot-finished steers. *Journal of Animal Science*, **79**:1032-1040.
- Amano, H., Kakinuma, M., Coury, D. A., Ohno, H., and Hara, T. 2005. Effect of seaweed mixtures on serum lipid level and platelet aggregation in rats. *Fisheries Science*, **71**(5): 1160-1166.
- Aneiros, A., Garateix, A. 2004. Bioactive peptides from marine sources: pharmacological properties and isolation procedures. *Journal of Chromatography B*, **803**(1): 41-53.
- AOAC International - Association of Official Analytical Chemists. 2000. Official Methods of Analysis of AOAC, Washington DC: AOAC International.
- Ariyoshi, Y. 1993. Angiotensin-converting enzyme-inhibitors derived from food proteins. *Trends in Food Science and Technology*, **4**(5): 139-144.
- Artan, M., Li, Y., Karadeniz, F., Lee, S. H., Kim, M. M., and Kim, S. K. 2008. Anti-HIV-1 activity of phloroglucinol derivative, 6,6'-bieckol, from *Ecklonia cava*. *Bioorganic and Medicinal Chemistry*, **16**(1): 7921-7926.
- Arvind, K. Hettiarachchy, N. S., and Mahedevan, M. 2012. Peptides derived from rice bran protect cells from obesity and alzheimer's disease. *International Journal of Biomedical Research*, **3**(3): 131-135.
- Athukorala, Y., and Jeon, Y. J. 2005. Screening for angiotensin-1-converting enzyme inhibitory activity of *Ecklonia cava*. *Journal of Food Science and Nutrition*, **10**(1): 134-139.
- Athukorala, Y., Lee, K. W., Kim, S. K., and Jeon, Y. J. 2007. Anticoagulant activity of marine green and brown algae collected from Jeju Island in Korea. *Bioresource Technology*, **98**(9): 1711-1716.
- Awad, N. E., Selim, M. A., Metawe, H. M., and Matloub, A. A. 2008. Cytotoxic xenicane diterpenes from the brown alga *Padina pavonia* (L.) Gaill. *Phytotherapy Research*, **22**(1): 1610-1613.
- Azwan, A., Karim, R. and Mitsui, T. 2010. Proteomic analysis of *Theobroma cacao* pod husk. *Journal of Applied Glycoscience*, **57**(1): 245-264.
- Bairoch, A. and Apweiler, R. 2000. The SWISS-PROT protein sequence database and its supplement TrEMBL in 2000. *Nucleic Acids Research*, **28**(1): 45-48.
- Barbarino, E. and Lourenco, S.O. 2005. An evaluation of methods for extraction and quantification of protein from marine macro- and microalgae. *Journal of Applied Phycology*, **17**(4): 47-460.

- Barsanti, L., and Gualtieri, P. 2006. *Algae: Anatomy, Biochemistry, and Biotechnology*. Boca Raton, FL: CRC Press, Taylor and Francis Group.
- Bergman, R.N., Finegood, D.T., and Kahn, S.E. 2002. The evolution of beta-cell dysfunction and insulin resistance in type 2 diabetes. *European Journal of Clinical Investigation*, **32**(3): 35-45.
- Berkelman, T. and Stenstedt, T. 1998. 2-D electrophoresis using immobilized pH gradients, Principles and Methods, Amersham Pharmacia Biotech Ltd.
- Bermejo, C., Garcı, R., Rodrı, J. M., Concepcio, D., Posas, F., and Arroyo, J. 2008. The sequential activation of the yeast hog and SLT2 pathways is required for cell survival to cell wall stress. *Molecular Biology of the Cell*, **19**(4):1113-1124.
- Bern, M., and Goldberg, D. 2006. *De novo* analysis of peptide tandem mass spectra by spectral graph partitioning. *Journal of Computational Biology*, **13**(1): 364-378.
- Bocanegra, A., Bastida, S., Benedi, J., Rodenas, S. and Sanchez-Muniz, F.J. 2009. Characteristics and nutritional and cardiovascular-health properties of seaweeds. *Journal of Medicinal Food*, **12**(1): 236-258.
- Boelsma, E. and Kloek, J. 2009. Lactotripeptides and antihypertensive effects: a critical review. *British Journal of Nutrition*, **101**: 776-786.
- Boguski, M. 1998. Bioinformatics, a new era. *Trends in Biotechnology*, **16**(S): 1-2.
- Bougatef, A., Nedjar-Arroume, N., Manni, L., Ravallec, R., Barkia, A., Guillochon, D. and Nasri, M. 2010. Purification and identification of novel antioxidant peptides from enzymatic hydrolysates of sardinelle (*Sardinella aurita*) by-products proteins. *Food Chemistry*, **118**(3): 559-565.
- Bradford, M.M. 1976. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Analytical Biochemistry*, **7**(1): 248-254.
- Brown, E. S., Allsopp, P. J., Magee, P. J., Gill, C. I. R., Nitecki, S., Strain, C. R., and McSorley, E. M. 2014. Seaweed and human health. *Nutrition Reviews*, **72**(3): 205-216.
- Brownlee, I., Seal, C., Wilcox, M., Dettmar, P., Pearson, J. and Rehm, B.H.A. 2009. Applications of alginate in food. *In: Alginates: Biology and Applications* (ed. B. H. Rehm), Springer: Berlin, Germany; pp. 211–228.
- Burtin, P. 2003. Nutritional value of seaweeds. *Electronic Journal of Environment Agriculture Food Chemistry*, **2**(1):498-503.

- Butler, M.S. 2004. The role of natural product chemistry in drug discovery. *Journal of Natural Products*, **67**(1): 2141-2153.
- Cao, X., Feng, J., Wang, D., Sun, J., Lu, X., and Liu, H. 2012. Primary style protein expression in the self-incompatible/compatible apricot by the 2D-DIGE technique. *Gene*, **503**(1): 110-117.
- Careri, M., Elviri, L., Lagos, J.B., Mangia, A., Speroni, F., and Terenghi, M. 2008. Selective and rapid immunomagnetic bead-based sample treatment for the liquid chromatography-electrospray ion-trap mass spectrometry detection of Ara h3/4 peanut protein in foods. *Journal of Chromatography A*, **1206**:89-94.
- Carlsson, A.S., Beilen, J.B.v., Möller, R., and Clayton, D., 2007. Micro- and macroalgae utility for industrial applications. *In: D. Bowles (Ed.), Output from the EPOBIO Project*. Newbury, UK: CPL Press.
- Carpentier, S.C., Panis, B., Vertommen, A., Swennen, R., Sergeant, K., Renaut, J., Laukens, K., Witters, E., Samyn, B., and Devreese, B. 2008. Proteome analysis of non-model plants: a challenging but powerful approach. *Mass Spectrometry Reviews*, **27**:354-377.
- Carpentier, S.C., Witters, E., Laukens, K., Deckers, P., Swennen, R. and Panis, B. 2005. Preparation of protein extracts from recalcitrant plant tissues: An evaluation of different methods for two-dimensional gel electrophoresis analysis. *Proteomics*, **5**(1): 2497-2507.
- Carrasco-Castilla, J., Hernández-Álvarez, A. J., Jiménez-Martínez, C., Gutiérrez-López, G. F., and Dávila-Ortiz, G. 2012. Use of proteomics and peptidomics methods in food bioactive peptide science and engineering. *Food Engineering Reviews*, **4**(4): 224-243.
- Carrasco-Castilla, J., Hernández-Álvarez, A. J., Jiménez-Martínez, C., Gutiérrez-López, G. F. and Dávila-Ortiz, G. 2012. Use of Proteomics and Peptidomics Methods in Food Bioactive Peptide Science and Engineering. *Food Engineering Reviews*, **4**(4): 224-243.
- Cengiz, S., Cavas, L., Yurdakoc, K., and Pohnert, G. 2011. The Sesquiterpene Caulerpenyne from *Caulerpa* spp. is a Lipoxygenase Inhibitor. *Marine Biotechnology*, **13**(2): 321-326.
- Cha, S. H., Ahn, G. N., Heo, S. J., Kim, K. N., Lee, K. W., Song, C. B., Cho, S. K. and Jeon, Y. J. 2006. Screening of extracts from marine green and brown algae in Jeju for potential marine angiotensin-I converting enzyme (ACE) inhibitory activity. *Journal of the Koreana Society of Food Science and Nutrition*, **35**: 307-314.
- Chakraborty, S. and Santra, S. C. 2008. Biochemical composition of eight benthic algae collected from Sunderban. *Indian Journal of Marine Sciences*, **37**(3): 329-332.

- Challapalli, K.K., Zabel, C., Schuchhardt, J., Kaindl, A.M., Klose, J., and Herzel, H. 2004. High reproducibility of large-gel two-dimensional electrophoresis. *Electrophoresis*, **25**: 3040-3047.
- Chandini, S. K., Ganesan, P., and Bhaskar, N. 2008. *In vitro* antioxidant activities of three selected brown seaweeds of India. *Food Chemistry*, **107**(2): 707-713.
- Chandramouli, K., and Qian, P.Y. 2009. Proteomics: challenges, techniques and possibilities to overcome biological sample complexity. *Human Genomics and Proteomics*, **204**:1-22.
- Chang, Y.W. and Alli, I. 2012. *In silico* assessment: suggested homology of chickpea (*Cicer arietinum* L.) legumin and prediction of ACE-inhibitory peptides from chickpea proteins using BLAST and BIOPEP analyses. *Food Research International*, **49**(1): 477-486.
- Chen, B., Dong, J.Q., Chen, Y.J., Wang, J.M., Tian, J., Wang, C.B., and Zou, S.Q. 2007. Two-dimensional electrophoresis for comparative proteomic analysis of human bile. *Hepatobiliary and Pancreatic Diseases International*, **6**(4):402-406.
- Cho, S. H., Lee, B. D., An, H., Eun, J. B. and Kenojeinin, I. 2005. Antimicrobial peptide isolated from the skin of the fermented skate, Raja kenoei. *Peptides*, **26**(4): 581-587.
- Cho, S. S., Lee, H. K., Yu, C. Y., Kim, M. J., Seong, E. S., Ghimire, B. K., Son, E. H., Chung, M. G., and Lim, J. D. 2008. Isolation and characterization of bioactive peptides from Hwangtae (yellowish dried Alaska pollack) protein hydrolysate. *Journal of Food Science and Nutrition*, **13**: 196-203.
- Cho, W.C. 2007. Proteomics technologies and challenges. *Genomics Proteomics Bioinformatics*, **5**(2):77-85.
- Chopin, T. and Sawhney, M. 2009. Seaweeds and their mariculture. *In: Encyclopedia of Ocean Sciences* (eds. J. H. Steele, S. Thorpe and K. Turekian), Elsevier Science: London, UK; pp. 317-326.
- Chynoweth, D. P., Owen, J. M. and Legrand, R. 2001. Renewable methane from anaerobic digestion of biomass. *Renewable Energy*, **22**: 1-8.
- Connan, S., Goulard, F., Stiger, V., Deslandes, E., and Gall, E. A. 2004. Interspecific and temporal variation in phlorotannin levels in an assemblage of brown algae. *Botanica Marina*, **47**(5): 410-416.
- Contreras, L., Dennett, G., Moenne, A., Palma, E. and Correa, J.A. 2007. Molecular and morphologically distinct *Scytosiphon* species (*Scytosiphonales*, *Phaeophyceae*) display similar antioxidant capacities. *Journal of Phycology*, **43**: 1320-1328.

- Contreras, L., Moenne, A., Gaillard, F., Potin, P. and Correa, J.A. 2010. Proteomic analysis and identification of copper stress-regulated proteins in the marine alga *Scytosiphon gracilis* (Phaeophyceae). *Aquatic Toxicology*, **96**: 85-89.
- Contreras, L., Ritter, A., Dennett, G., Boehmwald, F., Guitton, N., Pineau, C., Moenne, A., Potin, P., and Correa, J.A. 2008. Two-dimensional gel electrophoresis analysis of brown algal protein extracts. *Journal of Phycology*, **44**(1): 1315-1321.
- Corradini, E., Schmidt, P.J., Meynard, D., Garuti, C., Montosi, G., Chen, S., Vukicevic, S., Pietrangelo, A., Lin, H.Y., and Babitt, J.L. 2010. BMP6 treatment compensates for the molecular defect and ameliorates hemochromatosis in Hfe knockout mice. *Gastroenterology*, **139**: 1721-1729.
- Corthals, G.L., Wasinger, V.C., Hochstrasser, D.F. and Sanchez, J.C. 2000. The dynamic range of protein expression: a challenge for proteomic research. *Electrophoresis*, **21**: 1104-1115.
- Cox, S., Abu-Ghannam, N., and Gupta, S. 2010. An assessment of the antioxidant and antimicrobial activity of six species of edible Irish seaweeds. *International Food Research Journal*, **17**(1): 205-220.
- D'Alessandro, A. and Zolla, L. 2012. Food safety and quality control: Hints from proteomics. *Food Technology and Biotechnology*, **50**: 275-285.
- Da Silva, M.A.O., Garcia, J.S., de Souza, G.H.M.F., Eberlin, M.N., Gozzo, F.C., and Arruda, M.A.Z. 2010. Evaluation of sample preparation protocols for proteomic analysis of sunflower leaves. *Talanta*, **80**(4): 1545-1551.
- Damerval, C., Vienne, D.V., Zivy, M., and Thiellement, H. 1986. Technical improvements in two-dimensional electrophoresis increase the level of genetic variation detected in wheat-seedling proteins. *Electrophoresis*, **7**: 52-54.
- Darcy-Vrillon, B. 1993. Nutritional aspects of the developing use of marine macroalgae for the human food industry. *International Journal of Food Science and Nutrition*, **44**(1): 23-35.
- Darewicz, M., Dziuba, J., and Caessens, P.W.J.R. 2000. Effect of enzymatic hydrolysis on emulsifying and foaming properties of milk proteins – a review. *Polish Journal of Food Nutrition Science*, **9/50**(1): 3-8.
- Dass, C. 2007. Basics of mass spectrometry. *In: Fundamentals of contemporary mass spectrometry*. Hoboken, New Jersey: John Wiley and Sons, Inc., pp. 1-585.
- DATEX Working Group. 2009. Review of the potential health impact of beta-casomorphins and related peptides. *EFSA Science Report*, **231**:1-107.

- Dave, L.A., Montoya, C.A., Rutherford, S.M., and Moughan, P.J. 2014. Gastrointestinal endogenous proteins as a source of bioactive peptides-an *in silico* study. *PLoS One*, **9**(6): e98922.
- Davis, J., Sonesson, U., Baumgartner, D. U., and Nemecek, T. 2010. Environmental impact of four meals with different protein sources: Case studies in Spain and Sweden. *Food Research International*, **43**(1): 1874-1884.
- Dawczynski, C., Schubert, R., and Jahreis, G. 2007. Amino acids, fatty acids, and dietary fibre in edible seaweed products. *Food Chemistry*, **103**(3): 891-899.
- De Mejía, G. E., Martínez-Villaluenga, C., Fernández, D., Urado, D., and Sato, K. 2012. Bioavailability and safety of food peptides. *In: Food proteins and Peptides: Chemistry, Functionality Interactions, and Commercialization*. Hettiarachchy, N.S., Sato, K., Kannan, A., Editions. Taylor and Francis: Boca Raton, FL, USA. pp. 297-330.
- Des Francs, C.C., Thiellement, H., and De Vienne, D. 1985. Analysis of leaf proteins by two-Dimensional gel electrophoresis: Protease action as exemplified by ribulose biphosphate carboxylase/oxygenase degradation and procedure to avoid proteolysis during extraction. *Plant Physiology*, **78**: 178-182.
- Dhargalkar, V. K., and Pereira, N. 2005. Seaweed promising plant of the millennium. *Science and Culture*, **71**(1): 60-66.
- Dhargalkar, V.K., and Kavlekar, D. 2004. *Seaweeds - A field Manual Seaweeds*. National Institute of Oceanography, Dona Paula, Goa. pp. 1-42.
- Dickson-Spillman, M., Siegrist, M. and Keller, C. 2011. Attitudes toward chemicals are associated with preference for natural food. *Food Quality and Preference*, **22**(1): 149-156.
- Dowsey, B. A. W., and Yang, G. 2008. The future of large-scale collaborative proteomics, *Proceedings of the IEEE*, **96**(8): 1292-1309.
- Duan, L., Tsang, I., Xu, D., and Chua, T. 2009. Domain adaptation from multiple sources via auxiliary classifiers. *In: Proceedings of the 26<sup>th</sup> Annual International Conference on Machine Learning (ICML)*, Montreal, Canada, pp. 103-112.
- Duan, X. J., Zhang, W. W., Li, X. M., and Wang, B. G. 2006. Evaluation of antioxidant property of extract and fractions obtained from a red alga, *Polysiphonia urceolata*. *Food Chemistry*, **95**(1): 37-43.
- Dunn, M. J., and Görg, A. 2001. *Proteomics: From Protein Sequence to Function*. Oxford: BIOS Scientific Publishers, pp. 43-63.

- Dziuba J. and Iwaniak A., 2006. Database of bioactive peptide sequences. *in: Nutraceutical Proteins and Peptides in Health and Disease*. Ed. by CRC Press, pp. 543-564.
- Dziuba J., 2005. Research strategy for proteins and bioactive peptides. *In: Enzymatic modification of food components*. Eds E. Kołakowski, W. Bednarski, S. Bielecki. Wyd. AR Szczecin, pp. 219-237.
- Dziuba, J., Iwaniak, A., and Niklewicz, M. 2003. Database of protein and bioactive peptide sequences — BIOPEP. <http://www.uwm.edu.pl/biochemia>.
- Dziuba, J., Minkiewicz, P., Nałęcz, D., and Iwaniak, A., 1999. Database of biologically active peptide sequences. *Nahrung*, **43**: 190-195.
- Dziuba, J., Niklewicz, M., Iwaniak, A., Darewicz, M., and Minkiewicz, P. 2004. Bioinformatic-aided prediction for release possibilities of bioactive Peptides from plant proteins. *Acta Alimentaria Hungarica*, **33**(3): 227-235.
- Dziuba, M., Dziuba, B., and Iwaniak, A. 2009. Milk proteins as precursors of bioactive peptides. *Acta Scientiarum Polonorum Technologia Alimentaria*, **8**(1): 71-90.
- Eidhammer, I., Flikka, K., Martens, L., and Mikalsen, S.O. 2007. Protein identification and characterization by MS. *In: Computational Methods for Mass Spectrometry Proteomics*. John Wiley and Sons, Ltd. pp. 67-79.
- El Gamal, A.A. 2010. Biological importance of marine algae. *Saudi Pharmaceutical Journal*, **18** (1): 1-25.
- Eliason, B. C. 1998. Transient hyperthyroidism in a patient taking dietary supplements containing kelp. *The Journal of the American Board of Family Practice*, **11**(1): 478-480.
- Erdmann, K., Cheung, B.W., and Schröder, H. 2008. The possible roles of food-derived bioactive peptides in reducing the risk of cardiovascular disease. *The Journal of Nutritional Biochemistry*, **19**: 643-654.
- Eriksson, J., and Fenyo, D. 2005. Protein identification in complex mixtures research articles. *Journal of Proteome Research*, **4**: 387-393.
- Faurobert, M., Pelpoir, E., and Chaïb, J. 2007. Phenol extraction of proteins for proteomic studies of recalcitrant plant tissues. *Methods in Molecular Biology*, **355**: 9-14.
- Fenyö, D., and Beavis, R.C. 2008. Informatics development: challenges and solutions for MALDI mass spectrometry. *Mass Spectrometry Reviews*, **27**: 1-19.
- FitzGerald R. J. and Murray, B. A. 2006. Bioactive peptides and lactic fermentations. *International Journal of Dairy Technology*, **59**(1): 118-125.



- FitzGerald, C., Gallagher, E., Tasdemir, D. and Hayes, M. 2011. Heart health peptides from macroalgae and their potential use in functional foods. *Journal of Agricultural and Food Chemistry*, **59**(1): 6829–6836.
- FitzGerald, R. J., Murray, B. A. and Walsh, D. J. 2004. Hypotensive peptides from milk proteins. *The Journal of Nutrition*, **134**(4): 980S-988S.
- Fleurence, J. 1999. Seaweed proteins: biochemical, nutritional aspects and potential uses. *Trends in Food Science and Technology*, **10**(1): 25-28.
- Fleurence, J. 2004. Seaweed proteins. In: Yada, R. Y. [Ed.] *Proteins in Food Processing*. Woodhead Publishing Limited, Cambridge, UK. pp. 197-213.
- Fleurence, J., Massiani, L., Guyader, O., and Mabeau, S. 1995. Use of enzymatic cell wall degradation for improvement of protein extraction from *Chondrus crispus*, *Gracilaria verucosa* and *Palmaria palmata*. *Journal of Applied Phycology*, **7**: 393-397.
- Fong, P., Kamer, K., Boyer, K., and Boyle, K. 2001. Nutrient content of macroalgae with differing morphologies may indicate sources of nutrients for tropical marine systems. *Marine Ecology Progress Series*, **220**: 137-152.
- Fox, A. 2006. Mass Spectrometry for species or strain identification after culture or without culture: past, present, and future. *Journal of Clinical Microbiology*, **44**(1): 2677-2680.
- Fuchs, D., de Pascual-Teresa, S., Rimbach, G., Virgili, F., Ambra, R., Turner, R., Daniel, H. and Wenzel, U. 2005. Proteome analysis for identification of target proteins of genistein in primary human endothelial cells stressed with oxidized LDL or homocysteine. *European Journal of Nutrition*, **44**(1): 95-104.
- Fukudome, S., Jinsmaa, Y., Matsukawa, T., Sasaki, R., and Yoshikawa, M. 1997. Release of opioid peptides, gluten exorphins by the action of pancreatic elastase. *FEBS Letters*, **412**: 475-479.
- Galland-Irmouli, A., Fleurence, J., Lamghari, R., Luçon, M., Rouxel, C., and Barbaroux, O. 1999. Nutritional value of proteins from edible seaweed *Palmaria palmate* (Dulse). *Journal of Nutritional Biochemistry*, **10**(1): 353-359.
- Gallardo, J.M., Carrere, M., and Ortea, I. 2013. Proteomics in food science. *In: Foodomics: Advanced Mass Spectrometry in Modern Food Science and Nutrition*, 1<sup>st</sup> Edition. Edited by A. Cifuentes. John Wiley and Sons, Inc. pp. 125-165.
- Ghosh, T., Chattopadhyay, K., Marschall, M., Karmakar, P., Mandal, P., and Ray, B. 2009. Focus on antivirally active sulfated polysaccharides: From structure-activity analysis to clinical evaluation. *Glycobiology*, **19**(1): 2-15.

- Giavalisco, P., Nordhoff, E., Lehrach, H., Gobom, J., and Klose, J. 2003. Extraction of proteins from plant tissues for two dimensional electrophoresis analysis. *Electrophoresis*, **24**: 207-216.
- Gilani, G.S., Xiao, C., and Lee, N. 2008. Need for accurate and standardized determination of amino acids and bioactive peptides for evaluating protein quality and potential health effects of foods and dietary supplements. *Journal of AOAC International*, **91**(4): 894-900.
- Gilik, B. 2004. Identification of Seaweed Species in Selected Areas in the West and East Coasts of Sabah and their local used. Undergraduate thesis, Bachelor of Science-Marine Biology, Faculty of Science and Technology, University Malaysia Terengganu, Terengganu. pp. 141.
- Gingras, A.C., Aebersold, R., and Raught, B. 2005. Advances in protein complex analysis using mass spectrometry. *Journal of Physiology*, **563**: 11-21.
- Glazer, A.N. 1994. Phycobiliproteins: a family of valuable, widely used fluorophores. *Journal of Applied Phycology*, **6**(2): 105-112.
- Gobbetti, M., Minervini, F., and Rizzello, C.G. 2007. Bioactive peptides in dairy products. In: *Handbook of Food Products Manufacturing*, Y.H. Hui (ed). John Wiley and Sons, Inc., Hoboken, NJ. pp. 489-517.
- Gomez-Ordenez, E., Jimenez-Escrig, A., and Ruperez, P. 2010. Dietary fibre and physicochemical properties of several edible seaweeds from the northwestern Spanish coast. *Food Research International*, **43**(9): 2289-2294.
- Gomez-Vidal, S., Tena, M., Lopez-Llorca, L.V. and Salinas, J. 2008. Protein extraction from *Phoenix dactylifera* L. leaves, a recalcitrant material, for two-dimensional electrophoresis. *Electrophoresis*, **29**(1): 448-456.
- Görg, A., and Weiss, W. 2004. Current two-dimensional electrophoresis technology for proteomics. *Proteomics*, **12**: 3665–3685.
- Görg, A., Obermaier, C., Boguth, G., Harder, A., Scheibe, B., Wildgruber, R., and Weiss, W. 2000. The current state of two-dimensional electrophoresis with immobilized pH gradients. *Electrophoresis*, **21**(6): 1037-1053.
- Görg, A., Weiss, W. and Dunn, M.J. 2004. Current two-dimensional electrophoresis technology for proteomics. *Proteomics*, **4**(12): 3665-3685.
- Graham, L. and Wilcox, L. 2000. *Algae*. Prentice Hall: Upper Saddle River, CA, USA.
- Gressler, V., Fujii, M. T., Martins, A. P., Colepicolo, P., Mancini-Filho, J., and Pinto, E. 2011. Biochemical composition of two red seaweed species grown on the Brazilian coast. *Journal of the Science of Food and Agriculture*, **91**: 1687-1692.

- Grosso, C., Vinholes, J., Valentão, P., and Andrade, P. B. 2011. Halogenated compounds from seaweed, a biological overview. In: *Seaweed: Ecology, nutrient composition and medicinal uses*, F. Columbus (Ed.), New York, USA: Nova Science Publishers. pp. 1-25.
- Gu, R.-Z., Li, C.-Y., Liu, W.-Y., Yi, W.-X., and Cai, M.-Y. 2011. Angiotensin I-converting enzyme inhibitory activity of low-molecular-weight peptides from Atlantic salmon (*Salmo salar*) skin. *Food Research International*, **44**: 1536-1540.
- Guang, C., Phillips, R. D. 2009. Plant food-derived angiotensin I converting enzyme inhibitory peptides. *Journal of Agricultural and Food Chemistry*, **57**: 5113-5120.
- Gupta, S., and Abu-Ghannam, N. 2011. Bioactive potential and possible health effects of edible brown seaweeds. *Trends in Food Science and Technology*, **22**(6): 315-326.
- Gupta, S., Cox, S., and Abu-Ghannam, N. 2011. Effect of different drying temperatures on the moisture and phytochemical constituents of edible Irish brown seaweed. *LWT-Food Science and Technology*, **44**: 1266-1272.
- Gurib-fakim, A. 2006. Medicinal plants: Traditions of yesterday and drugs of tomorrow. *Molecular Aspects of Medicine*, **27**: 1-93.
- Gygi, S.P. and Aebersold, R. 2000. Mass spectrometry and proteomics. *Current Opinion in Chemical Biology*, **4**(1): 489-494.
- Hagopian, J. C., Reis, M., Kitajima, J. P., Bhattacharya, D. and Oliveira, M. C. 2004. Comparative analysis of the complete plastid genome sequence of the red alga *Gracilaria tenuistipitata* var. *liui* provides insights into the evolution of rhodoplasts and their relationship to other plastids. *Journal of Molecular Evolution*, **59**(1): 464-77.
- Harnedy, P. A., and FitzGerald, R. J. 2011. Bioactive proteins, peptides, and amino acids from macroalgae. *Journal of Phycology*, **47**(2): 218-232.
- Harnedy, P. A., and FitzGerald, R. J. 2013. Bioactive Proteins and Peptides from Macroalgae, Fish, Shellfish and Marine Processing Waste. *Marine Proteins and Peptides: Biological Activities and Applications*, First Edition. Edited by Se-Kwon Kim. John Wiley and Sons, Ltd. pp.5-39.
- Hartmann, R., and Meisel, H. 2007. Food-derived peptides with biological activity: from research to food applications. *Current Opinion in Biotechnology*, **18**(2): 163-169.
- Haynes, C.M., Petrova, K., Benedetti, C., Yang, Y., and Ron, D. 2007. ClpP mediates activation of a mitochondrial unfolded protein response in *C. elegans*. *Developmental Cell*, **13**: 467-480.

- He, H.L., Chen, X.L., Wu, H., Sun, C.Y., Zhang, Y.Z., and Zhou, B.C. 2007. High throughput and rapid screening of marine protein hydrolysates enriched in peptides with angiotensin-I-converting enzyme inhibitory activity by capillary electrophoresis. *Bioresource Technology*, **98**: 3499-3505.
- Hemmingson, J. A., Falshaw, R., Furneaux, R. H., and Thompson, K. 2006. Structure and antiviral activity of the galactofucan sulfates extracted from *Undaria pinnatifida* (Phaeophyta). *Journal of Applied Phycology*, **18**(1): 185-193.
- Henning, L. 1999. WinGene/WinPep: User-friendly software for the analysis of amino acid sequences. *Bio Techniques*, **26**: 1170-1172.
- Heo, S. J. and Jeon, Y. J. 2008. Radical scavenging capacity and cytoprotective effect of enzymatic digests of *Ishige okumurae*. *Journal of Applied Phycology*, **20**: 1087-1095.
- Heo, S. J., Ko, S. C., Cha, S. H., Kang, D. H., Park, H. S., Choi, Y. U., Kim, D., Jung, W.K., and Jeon, Y.J. 2009. Effect of phlorotannins isolated from *Ecklonia cava* on melanogenesis and their protective effect against photo-oxidative stress induced by UV-B radiation. *Toxicology in Vitro*, **23**: 1123-1130.
- Hogan, S., Zhang, L., Li, J., Wang, H. and Zhou, K. 2009. Development of antioxidant rich peptides from milk protein by microbial proteases and analysis of their effects on lipid peroxidation in cooked beef. *Food Chemistry*, **117**(3): 438-443.
- Holanda, M. L., Pereira, M. G., and Biologia, D. 2005. Differential activity of a lectin from *Solieria filiformis* against human pathogenic bacteria. *Brazilian Journal of Medical and Biological Research*, **38**: 1769-1773.
- Holdt, S. L., and Kraan, S. 2011. Bioactive compounds in seaweed: functional food applications and legislation. *Journal of Applied Phycology*, **23**(3): 543-597.
- Hong, F., Ming, L., Yi, S., Zhanxia, L., Yongquan, W., and Chi, L. 2008. The antihypertensive effect of peptides: a novel alternative to drugs. *Peptides*, **29**: 1062-1071.
- Horrocks, L.A. and Yeo, Y.K. 1999. Health benefits of do-cosahexaenoic acid(DHA). *Pharmacology Research*, **40**(3): 211-225.
- Horstmann, C. 1983. Specific subunit pairs of legumin from *Vicia faba*. *Phytochemistry*, **22**: 1861-1866.
- Hui, Y. H. 1992. Cholesterol and heart disease. *Irr.* Y. H. Hui (Ed.), *Encyclopedia of Food Science and Technology*, New York: Wiley-Interscience publication. Vol. 3, pp. 2043-2047.

- Hurkman, W. J., and Tanaka, C. K. 2007. Extraction of wheat endosperm proteins for proteome analysis. *Journal of Chromatography B*, **849**(1-2): 344-50.
- Hurkman, W.J., and Tanaka, C.K. 1986. Solubilization of plant membrane proteins for analysis by two-dimensional gel electrophoresis. *Plant Physiology*, **81**: 802-806.
- Ibanez, E., Herrero, M., Mendiola, J.A., and Castro-Puyana, M. 2012. *Irr. Marine Bioactive Compounds: Sources, Characterization and Applications* (ed M. Hayes), Springer, pp. 55-98.
- Inagaki, N. and Katsuta, K. 2004. Large gel two-dimensional electrophoresis: improving recovery of cellular proteome. *Current Proteomics*, **1**: 35-39.
- Iso H. 2011. Lifestyle and cardiovascular disease in Japan. *Journal of Atherosclerosis and Thrombosis*, **18**: 83-88.
- Ito, K., and Hori, K. 1989. Seaweed: chemical composition and potential uses. *Food Review International*, **5**(1): 101-144.
- Iwaniak A., and Dziuba J., 2011. *BIOPEP-PBIL tool in analysis of the structure of biologically active motifs from food proteins. Food Technology and Biotechnology*, **49**(1): 118-127.
- Iwaniak, A., and Dziuba, J. 2009. Motifs with potential physiological activity in food proteins-BIOPEP database. *ACTA Scientiarum Polonorum, Technologia Alimentaria*, **8**(3): 59-85.
- Iwaniak, A., Dziuba, J., and Niklewicz, M. 2005. The BIOPEP database-a tool for the *in silico* method of classification of food proteins as the source of peptides with antihypertensive activity. *Acta Alimentaria*, **34**(4): 417-425.
- Jacobs, D.I., Van Rijssen, M.S.R., Van Der Heijden, R.R., and Verpoorte, R. 2001. Sequential solubilization of proteins precipitated with trichloroacetic acid in acetone from cultured *Catharanthus roseus* cells yields 52% more spots after two-dimensional electrophoresis. *Proteomics*, **1**:1345-1350.
- Je, J. Y., Park, P. J., Kim, E. K., Park, J. S., Yoon, H. D., Kim, K. R. and Ahn, C. B. 2009. Antioxidant activity of enzymatic extracts from the brown seaweed *Undaria pinnatifida* by electron spin resonance spectroscopy. *LWT Food Science and Technology*, **42**:874-878.
- Jha, R. K. and Zi-rong, X. 2004. Biomedical compounds from marine organisms. *Marine Drugs*, **2**(1): 123-146.
- Jones, W.P., Chin, Y.W. and Kinghorn, A.D. 2006. The role of pharmacognosy in modern medicine and pharmacy. *Current Drug Targets*, **7**(1): 247-264.

- Jorrín-nova, J.V., Maldonado, A.M., Echevarría-Zomeño, S., valledor, L., Castillejo, M.A., Curto, M., Valero, J., Sghaier, B., Donoso, G., and Redondo, I. 2009. Plant proteomics update (2007–2008): second-generation proteomic techniques, an appropriate experimental design, and data analysis to fulfill miAPe standards, increase plant proteome coverage and expand biological knowledge. *Journal of Proteomics*, **72**: 285-314.
- Jung, E., Heller, M., Sanchez, J.C., and Hochstrasser, D.F. 2000. Proteomics meets cell biology: the establishment of subcellular proteomes. *Electrophoresis*, **21**: 3369-3377.
- Kaehler, S., and Kennish, R. 1996. Summer and winter comparisons in the nutritional value of marine macroalgae from Hong Kong. *Botanica Marina*, **39**(1): 11-17.
- Kaledona, M.M., Reneta, A., Toshkova, Elena, G.G., Magdalena, I.T., Natalia, J.I., Liliya, S.Y., and Liliana, G.G. 2011. Antitumor activity of B-phycoerythrin from *Porphyridium cruentum*. *Journal of Pharmacy Research*, **4**(5): 1480-1482.
- Kaliaperumal, N. 2003. Products from seaweeds. *SDMRI Research Publication*, **3**: 33-42.
- Karelin, A.A., Blishchenko, E.Y., and Ivanov, V.T. 1998. A novel system of peptidergic regulation. *FEBS Letters*, **428**: 7-12.
- Khan, M. N. A., Cho, J. Y., Lee, M. C., Kang, J. Y., Park, N. G., Fujii, H., and Hong, Y. K. 2007. Isolation of two anti-inflammatory and one pro-inflammatory polyunsaturated fatty acids from the brown seaweed *Undaria pinnatifida*. *Journal of Agricultural and Food Chemistry*, **55**(17): 6984-6988.
- Khan, S. I. and Satam, S. B. 2003. Seaweed mariculture: scope and potential in India. *Aquaculture Asia Magazine*, October–December: 26-29.
- Kim, E.Y., Kim, D.G., Kim, Y.R., Hwang, H.J., Nam, T.J. and Kong, I.S. 2011 An improved method of protein isolation and proteome analysis with *Saccharina japonica* (Laminariales) incubated under different pH conditions. *Journal of Applied Phycology*, **23**(1): 123-130.
- Kim, S. K., and Wijesekara, I. 2010. Development and biological activities of marine-derived bioactive peptides: a review. *Journal of Functional Foods*, **2**: 1-9.
- Kim, S.K. and Mendis, E. 2006. Bioactive compounds from marine processing byproducts a review. *Food Research International*, **39**(1): 383-93.
- Kim, S.T., Cho, K.S., Jang, Y.S., and Kang, K.Y. 2001. Two-dimensional electrophoretic analysis of rice proteins by polyethylene glycol fractionation for protein arrays. *Electrophoresis*, **22**: 2103-2109.

- Kinter, M. and N. Sherman. 2000. The primary structure of protein and a historical overview of protein sequencing. *Protein Sequencing and Identification Using Tandem Mass Spectrometry*. New York: Wiley-Interscience, pp. 6-22.
- Klose, J. 1975. Protein mapping by combined isoelectric focusing and electrophoresis of mouse tissues. A novel approach to testing for induced point mutation in mammals. *Human genetic*, **26**(1): 231-243.
- Koehn, F.E. 2006. Therapeutic potential of natural product signal transduction agents. *Current Opinion in Biotechnology*, **17**(1): 631-637.
- Koehn, F.E. and Carter, G.T. 2005. The evolving role of natural products in drug discovery. *Nature Reviews Drug Discovery*, **4**(1): 206-220.
- Komajda, M. and Wilmart, M. C. 2000. Angiotensin converting enzyme inhibition: from viper to patient. *Heart*, **84**(1): I11-I14.
- Kong, C. S., Kim, J. A., Yoon, N. Y., and Kim, S. K. 2009. Induction of apoptosis by phloroglucinol derivative from *Ecklonia Cava* in MCF- 7 human breast cancer cells. *Food and Chemical Toxicology*, **47**: 1653-1658.
- Korhonen H., Pihlanto, A., Rantamäki P., and Tupasela T. 1998. Impact of processing on bioactive proteins and peptides. *Trends in Food Science and Technology*, **9**: 307-319.
- Korhonen, H. 2009. Milk-derived bioactive peptides: From science to applications. *Journal of Functional Foods*, **1**(2): 177-187.
- Korhonen, H. and Pihlanto, A. 2003. Food-derived bioactive peptides-opportunities for designing future foods. *Current Pharmaceutical Design*, **9**(16): 1297-1308.
- Korhonen, H., and Pihlanto, A. 2007. Technological options for the production of health-promoting proteins and peptides derived from milk and colostrum. *Current Pharmaceutical Design*, **13**: 829-843.
- Korhonen, H., and Pihlanto, A., 2006. Bioactive peptides: production and functionality. *International Dairy Journal*, **16**: 945-960.
- Kruger, N.J. 2002. The Bradford method for protein quantitation. *The Protein Protocols Handbook*, **1**: 16-20.
- Kumar, M., Kumari, P., Gupta, V., Reddy, C.R.K. and Jha, B. 2010. Biochemical responses of red alga *Gracilaria corticata* (Gracilariales, Rhodophyta) to salinity induced oxidative stress. *Journal of Experimental Marine Biology and Ecology*, **391**: 27-34.
- Kuwana, R., Kasahara, Y., Fujibayashi, M., Takamatsu, H., Ogasawara, N. and Watabe, K. 2002. Proteomics characterization of novel spore proteins of *Bacillus subtilis*. *Microbiology*, **148**(1): 3971-3982.

- Lacroix, I.M.E., and Li-Chan, E.C.Y. 2012. Evaluation of the potential of dietary proteins as precursors of dipeptidyl peptidase (DPP)-IV inhibitors by an *in silico* approach. *Journal of Functional Foods*, **4**: 403-422.
- Laemmli, U.K. 1970. Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature*, **227**(1): 680-685.
- Lahaye, M. 1993. Marine algae as a source of dietary fibers: Determination of soluble and insoluble dietary fibre contents in some 'sea vegetable'. *Journal of the Science of Food and Agriculture*, **54**(1): 523-535.
- Lamond, A.I., Uhlen, M., Horning, S., Makarov, A., Robinson, C.V., Serrano, L., Hartl, F.U., Baumeister W, Werenskiold AK, Andersen JS, Vorm O, Linial M, Aebersold R., and Mann, M. 2012. Advancing cell biology through proteomics in space and time (PROSPECTS). *Molecular and Cell Proteomics*, **11**(3):O112.
- Latham, P.W. 1999. Therapeutic peptides revisited. *Nature Biotechnology*, **17**: 755-758.
- Lederberg, J., and McCray, A.T. 2001. 'Ome Sweet' Omics - A Genealogical Treasury of Words Genealogical Treasury of Words. *Scientist*, **15**(7):8-10.
- Lee, J. B., Hayashi, K., Hashimoto, M., Nakano, T., and Hayashi, T. 2004. Novel antiviral fucoidan from sporophyll of *Undaria pinnatifida* (Mekabu). *Chemical and Pharmaceutical Bulletin*, **52**(9): 1091-1094.
- Lee, S. H., Qian, Z. J., and Kim, S. K. 2010. A novel angiotensin I converting enzyme inhibitory peptide from tuna frame protein hydrolysate and its antihypertensive effect in spontaneously hypertensive rats. *Food Chemistry*, **118**: 96-102.
- Levine, H.G. 1984. The use of seaweeds for monitoring coastal waters. *Irr. Algae as Ecological Indicators*, L.E. Shubert (ed.), Academic Press, London, New York. pp. 188-210.
- Li, Y.X. and Kim, S.K. 2011. Utilization of seaweed derived ingredients as potential antioxidants and functional ingredients in the food industry: an overview. *Food Science and Biotechnology*, **20**(1): 1461-1466.
- Lim, H. T., and Teo, S. S. 2015. Comparison of protein extraction protocols for proteomic analysis of red algae, *Eucheuma cottonii*. *Pertanika Journal of Tropical Agricultural Science*, **38**(2): 279-293.
- Lim, S. N., Cheung, P. C. K., Ooi, V. E. C., and Ang, P. O. 2002. Evaluation of antioxidative activity of extracts from a brown seaweed, *Sargassum siliquastrum*. *Journal of Agricultural and Food Chemistry*, **50**(13): 3862-3866.
- Lönnerdal B. 2002. Bioactive proteins: clinical applications for gastrointestinal health. *Bulletin of International Dairy Federation*, **375**:22-24.



- Lopez, E.I., and Recio, I. 2006. Antibacterial activity of peptides and folding variants from milk proteins. *International Dairy Journal*, **16**: 1294-1305.
- Lourenço, S.O., Barbarino, E., De-Paula, J.C., Freitas, J.N.P., and Diniz, G.S. 2006. Tissue nitrogen and phosphorus in seaweeds in a tropical eutrophic environment: What a long-term study tells us. *Journal of Applied Phycology*, **18**:389-398.
- Lu, Q., Lu, J.P., Li, X.D., Liu, X.H., Min, H., and Lin, F.C. 2008. *Magnaporthe oryzae* MTP1 gene encodes a type III transmembrane protein involved in conidiation and conidial germination. *Journal of Zhejiang University Science B*, **9**(7): 511-519.
- Majumder, K. and Wu, J. 2010. A new approach for identification of novel antihypertensive peptides from egg proteins by QSAR and bioinformatics. *Food Research International*, **43**(5): 1371-1378.
- Majumder, K., and Wu, J. 2009. Angiotensin I converting enzyme inhibitory peptides from mimic *in vitro* gastrointestinal digestion of cooked eggs. *Journal of Agricultural and Food Chemistry*, **57**: 471-477.
- Malafaia, C. B., Guerra, M. L., Silva, T. D., Paiva, P. M. G., Souza, E. B., Correia, M. T. S., and Silva, M. V. 2015. Selection of a protein solubilization method suitable for phytopathogenic bacteria: a proteomics approach. *Proteome Science*, **13**(5):1-7.
- Manivannan, K., Thirumaran, G., Devi, G. K., Anantharaman, P., and Balasubramanian, T. 2009. Proximate composition of different group of seaweeds from vedalai coastal waters (Gulf of Mannar): Southeast Coast of India. *Middle East Journal of Scientific Research*, **4**(2): 72-77.
- Mao, G., Meng, X., Liu, Y., Zheng, Z., Chen, Z., and Zhang, S. 2011. Phosphorylation of a WRKY transcription factor by two pathogen-responsive MAPKs drives phytoalexin biosynthesis in Arabidopsis. *The Plant Cell*, **23**: 1639-1653.
- Marengo, E., Robotti, E., Antonucci, F., Cecconi, D., Campostrini, N., and Righetti, P.G. 2005. Numerical approaches for quantitative analysis of two-dimensional maps: a review of commercial software and home-made systems. *Proteomics*, **5**: 654-666.
- Marinho-Soriano, E., Fonseca, P. C., Carneiro, M. A. A., and Moreira, W. S. C. 2006. Seasonal variation in the chemical composition of two tropical seaweeds. *Bioresource Technology*, **97**(18): 2402-2406.

- Marko-Varga, G., Lindberg, H., Lofdahl, C.G., Jonsson, P., Hansson, L., Dahlback, M., Lindquist, E., Johansson, L., Foster, M., and Fehniger, T.E. 2005. Discovery of biomarker candidates within disease by protein profiling: Principles and concepts. *Journal of Proteome Research*, **4**(4): 1200-1212.
- Marsham, S., Scott, G.W. and Tobin, M.L. 2007. Comparison of nutritive chemistry of a range of temperate seaweeds. *Food Chemistry*. **100**: 1331-1336.
- Martinez, B., and Rico, J.M. 2002. Seasonal variation of P content and major N pools in *Palmaria palmate* (Rhodophyta). *Journal of Phycology*, **38**: 1082-1089.
- Martínez-Aragón, J.F., Hernández, I., Pérez-Looréns, J.L., Vázquez, R., and Vergara, J.J. 2002. Biofiltering Efficiency in Removal of Dissolved Nutrients by Three Species of Estuarine Macroalgae Cultivated with Sea Bass (*Dicentrarchus labrax*) Waste Waters 1. Phosphate. *Journal of Applied Phycology*, **14**(5): 365-374.
- Mary, A., Mary, V., Lorella, A. and Matias, J.R. 2009. Rediscovery of naturally occurring seagrape *Caulerpa lentillifera* from the Gulf of Mannar and its mariculture. *Current Science*, **97**(10): 1418-1420.
- Matanjan, P., Mohamed, S., Mustapha, N.M. and Muhammad, K. 2009. Nutrient content of tropical edible seaweeds, *Euclima cottonii*, *Caulerpa lentillifera* and *Sargassum polycystum*. *Journal of Applied Phycology*, **21**(1): 75-80.
- Matanjan, P., Mohamed, S., Mustapha, N.M., Muhammad, K., and Ming, C.H. 2008. Antioxidant activities and phenolics content of eight species of seaweeds from north Borneo. *Journal of Applied Phycology*, **20**(1): 367-373.
- Matsukawa, R., Dubinsky, Z., Kishimoto, E., Masaki, K., Masuda, Y., Takeuchi, T., Chihara, M., Yamamoto, Y., Niki, E., and Karube, I. 1997. A comparison of screening methods for antioxidant activity in seaweeds. *Journal of Applied Phycology*, **9**(1): 29-35.
- Matsumura, Y. 2001. Nutrition trends in Japan. *Asia Pacific Journal of Clinical Nutrition*, **10**(1):S40-S47.
- Matta, C.B.B., Da Matta C.B., Souza E.T., Queiroz A.C., Lira D.P., Araújo M.V., Cavalcante-Silva L.H. De Miranda, G.E., De Araujo-Junior, J.X., Barbosa-Filho, J.M., De Oliveira Santos, B.V., and Alexandre-Moreira, M.S. 2011. Antinociceptive and anti-inflammatory activity from algae of the genus *Caulerpa*. *Marine Drugs*, **9**(12): 307-318.
- McDermid, K.J., and Stuercke, B. 2003. Nutritional composition of edible Hawaiian seaweeds. *Journal of Applied Phycology*, **15**(6): 513-524.

- McHugh, D.J. 1991. Worldwide distribution of commercial resources of seaweeds including Gelidium. *Hydrobiologia*, **221**: 19–29.
- McHugh, D.J. 2003. A guide to the seaweed industry. *FAO Fish Technical Paper 441*, Rome, Italy, pp.105.
- Medina, M., Andrade, S., Faugeron, S., Lagos, N., Mella, D. and Correa, J.A. 2005. Biodiversity of rocky intertidal benthic communities associated with copper mine tailing discharges in northern Chile. *Marine Pollution Bulletin*, **50**: 396-409.
- Mehta, A., Brasileiro, A.C., Souza, D.S., Romano, E., Campos, M.A., Grossi-de-Sá, M.F., Silva, M.S., Franco, O.L., Fragoso, R.R., Bevitori, R. and Rocha, T.L. 2008. Plant-pathogen interactions: what is proteomics telling us. *FEBS Journal*, **275**: 3731-3746.
- Meisel, H. 2005. Biochemical properties of peptides encrypted in bovine milk proteins. *Current Medicinal Chemistry*, **12**: 1905-1919.
- Meisel, H., 1998. Overview on milk protein derived peptides. *International Dairy Journal*, **8**: 363-373.
- Meisel, H., Fitzgerald, R. J., and Milchforschung, E. 2000. Opioid peptides encrypted in intact milk protein sequences. *British Journal of Nutrition*, **84**(1): 27-31.
- Mendis, E., Rajapakse, N., Byun, H. G. and Kim, S. K. 2005. Investigation of jumbo squid (*Dosidicus gigas*) skin gelatin peptides for their *in vitro* antioxidant effects. *Life Sciences*, **77**(17): 2166-2178.
- Mendis, E and Kim, S.K. 2011. Present and Future Prospects of Seaweeds in Developing Functional Foods. *In: Advances in Food and Nutrition Research, Volume 64: Marine Medicinal Foods; Implications and Applications, Macro and Microalgae*, Elsevier Inc. USA. pp. 1-13.
- Mine, Y, and Shahidi, F. 2006. Nutraceutical Proteins and Peptides in Health and Disease: An Overview. *In: Nutraceutical Proteins and Peptides in Health and Disease*, Y. Mine, F. Shahidi (Eds.), CRC Press, Boca Raton, FL, USA, pp. 3.
- Mine, Y., Li Chan, E. C. Y., and Jiang, B. 2010. Biologically active food proteins and peptides in health. *In: Bioactive Proteins and Peptides as Functional Foods and Nutraceuticals*, Blackwell Publishing Ltd. pp 3-11.
- Mischak, H., Apweiler, R., Banks, R.E., Conaway, M., Coon, J., Dominiczak, A., Ehrich, J.H.H., Fliser, D., Girolami, M., Hermjakob, H., Hochstrasser, D., Jankowski, J., Julian, B.A., Kolch, W., Massy, Z.A., Neusuess, C., Novak, J., Peter, K., Rossing, K., Schanstra, J., Semmes, O.J., Theodorescu, D., Thongboonkerd, V., Weissinger, Van Eyk J.E., and Yamamoto, T. 2007. Clinical proteomics: A need to define the field and to begin to set adequate standards. *Proteomics-Clinical Applications*, **1**(2): 148-156.

- Mišurcován, L. Kracmar, S., Klejdus, B., and Vacek, J. 2010. The mineral content of products from freshwater algae and seaweed (in Czech). *Czech Journal of Food Science*, **20**(1): 27-35.
- Mohamed, S., Hashim, S.N. and Rahman, H.A. 2012. Seaweeds: a sustainable functional food for complementary and alternative therapy. *Trends in Food Science and Technology*, **23**: 83-96.
- Möller, N. P., Scholz-Ahrens, K. E., Roos, N., and Schrezenmeir, J. 2008. Bioactive peptides and proteins from foods: Indication for health effects. *European Journal of Nutrition*, **47**(4): 171-182.
- Moreno, J.J. and Mitjawila, M.T. 2003. The degree of unsaturation of dietary fatty acids and the development of atherosclerosis (review). *Journal of Nutritional Biochemistry*, **14**: 182-195.
- Moy, F.E. and M. Walday, 1996. Accumulation and depuration of organic micro-pollutants in marine hard bottom organisms. *Marine Pollution Bulletin*, **33**: 56-63.
- Murata, M., and Nakazoe, J. 2001. Production and use of marine algae in Japan. *Jarq-Japan Agricultural Research Quarterly*, **35**(4): 281-290.
- Murty, S.U., and Banerjee, A.K. 2011. Seaweeds: The wealth of oceans. *Handbook of Marine Macroalgae: Biotechnology and Applied Phycology*, John Wiley and Sons, Ltd. Pp.36-44.
- Nagai, K., Yotsukura, N., Ikegami, H., Kimura, H., and Morimoto, K. 2008. Protein extraction for 2-DE from lamina of *Ecklonia kurome* (laminariales): Recalcitrant tissue containing high levels of viscous polysaccharides. *Electrophoresis*, **29**: 672-681.
- Nagayama, K., Iwamura, Y., Shibata, T., Hirayama, I., and Nakamura, T. 2002. Bactericidal activity of phlorotannins from the brown alga *Ecklonia kurome*. *Journal of Antimicrobial Chemotherapy*, **50**(1): 889-893.
- Newman, D.J., Cragg, G.M., Holbeck, S. and Sausville, E.A. 2002. Natural products and derivatives as leads to cell cycle pathway targets in cancer chemotherapy. *Current Cancer Drug Targets*, **2**(1): 279-308.
- Ngo, D.H., Vo, T.S., Ngo, D.N., Wijesekara, I., and Kim, S.K. 2012. Biological activities and potential health benefits of bioactive peptides derived from marine organisms. *International Journal of Biological Macromolecules*, **51**:378-83.
- Nielsen K.J. 2007. Algae, Overview. In: *Encyclopedia of Tidepools and Rocky Shores*, By M. W. Denny and S. D. Gaines. University of California Press, California. pp. 10-21.

- Noiraksar, T., Ajisaka, T., and Agardh, S.C.A. 2008. Taxonomy and distribution of *Sargassum* (Phaeophyceae) in the Gulf of Thailand, Borowitzka (eds.), *Nineteenth International Seaweed Symposium*, **20**(5): 513-527.
- Norziah, M.H. and Ching, C.H.Y. 2000. Nutritional composition of edible seaweed *Gracilaria changgi*. *Food Chemistry*, **68**: 69-76.
- O'Connor, J. and Warwicker, J. 1998. Prediction of peptides in the fermented cocoa storage protein with reference to the modelled 3D structure. *Journal of the Science of Food and Agriculture*, **77**: 109-114.
- O'Farrell, P.H. 1975. High resolution two-dimensional electrophoresis of proteins. *The Journal of Biological Chemistry*, **250**(1): 4007-4021.
- Ohsawa, K., Satsu, H., Ohki, K., Enjoh, M., Takano, T., and Shimizu, M. 2008. Producibility and digestibility of antihypertensive b-casein tripeptides, Val-pro-pro and ile-pro-pro, in the gastrointestinal tract: Analyses using an *in vitro* model of mammalian gastrointestinal digestion. *Journal of Agricultural Food Chemistry*, **56**: 854-858.
- Oliveira, E.C., Corbisier, T.N., de Eston, V.R. and Ambrosio, O. 1997. Phenology of a seagrass (*Halodule wrightii*) bed on the southeast coast of Brazil. *Aqua Botanica*, **56**: 25-33.
- Ortiz, J., Romero, N., Robert, P., Araya, J., Lopez-Hernandez, J., Bozzo, C., Navarrete, E., Osorio, A., and Rios, A. 2006. Dietary Fiber, Amino Acid, Fatty Acid and Tocopherol Contents of the Edible Seaweeds *Ulva lactuca* and *Durvillaea antarctica*. *Food Chemistry*, **99**(1): 98-104.
- Ovalle, A.R.C., Rezende, C.E., Carvalho, C.E.V., Jennerjahn, T.C. and Ittekkot, V. 1999. Biogeochemical characteristics of coastal waters adjacent to small river-mangrove systems, East Brazil. *Geo-Marine Letters*, **19**: 179-185.
- Ozdemir, V., Armengaud, J., Dub'e, L., Aziz, R.K., and Knoppers, B.M. 2010. Nutriproteomics and proteogenomics: cultivating two novel hybrid fields of personalized medicine with added societal value. *Current Pharmacogenomics and Personalized Medicine*, **8**: 240-244.
- Pampanin, D. M., Larssen, E., Provan, F., Sivertsvik, M., Ruoff, P., and Sydnes, M. O. (2012). Detection of small bioactive peptides from Atlantic herring (*Clupea harengus* L.). *Peptides*, **34**(2): 42-36.
- Pandey, A., and Mann, M. 2000. Proteomics to study genes and genomes. *Nature*, **405**(6788): 837-846.
- Pangestuti, R. and Kim, S. 2011. Biological activities and health benefit effects of natural pigments derived from marine algae. *Journal of Functional Foods*, **3**(4): 255-266.

- Park, C.B., Kim, M.S., and Kim, S.C., 1996. A novel antimicrobial peptide from *Bufo gargarizans*. *Biochemical and Biophysical Research Communications*, **218**(1): 408-413.
- Patier, P., Yvin, J.-C., Kloareg, B., Li' enar, Y., and Rochas, C. 1993. Seaweed liquid fertilizer from *Ascophyllum nodosum* contains elicitors of plant D-glycanases. *Journal of Applied Phycology*, **5**: 343-349.
- Patterson, S. D. and Aebersold, R. H. 2003. Proteomics: the first decade and beyond. *Nature Genetics Supplements*, **33**: 311-323.
- Patterson, S.D. 2004. How much of the proteome do we see with discovery-based proteomics methods and how much do we need to see? *Current Proteomics*, **1**: 3-12.
- Paul, N. A., Neveux, N., Magnusson, M., and De Nys, R. 2014. Comparative production and nutritional value of sea grapes - the tropical green seaweeds *Caulerpa lentillifera* and *C. racemosa*. *Journal of Applied Phycology*, **26**(4): 1833-1844.
- Pavokovic, D., Kriznik, B., and Rasol, M.K. 2012. Evaluation of protein extraction methods for proteomic analysis of non-model recalcitrant plant tissues. *Croatica Chemica Acta*, **85**(2): 177-183.
- Pedreschi, R., Hertogi, M., Lilley, K.S., and Nicolai, B. 2010. Proteomics for the food industry: opportunities and challenges. *Critical Review in Food Science and Nutrition*, **50**: 680-692.
- Pereira, H. S., Leao-Ferreira, L. R., Moussatch, N., Teixeira, V. L., Cavalcanti, D. N., Costa, L. J., Diaz, R., and Frugulhetti, I.C. 2004. Antiviral activity of diterpenes isolated from the Brazilian marine alga *Dictyota menstrualis* against human immunodeficiency virus type 1 (HIV-1). *Antiviral Research*, **64**(1): 69-76.
- Phang, S.M. 2006. Seaweed resources in Malaysia: Current status and future prospects. *Aquatic Ecosystem Health and Management*, **9**(2): 185-202.
- Phang, S.M. 2010. Potential products from tropical algae and seaweeds, especially with reference to Malaysia. *Malaysian Journal of Science*, **29**(2): 160-166.
- Phelan, M., Aherne, A., Fitzgerald, R.J. and O'Brien, N.M. 2009. Casein-derived bioactive peptides: biological effects, industrial uses, safety aspects and regulatory status. *International Dairy Journal*, **19**: 643-654.
- Phillips, D.J.H., 1995. The chemistries and environmental fates of trace metals and organochlorines in aquatic ecosystems. *Marine Pollution Bulletin*, **31**: 193-200.

- Pihlanto, A. 2006. Antioxidative peptides derived from milk proteins. *International Dairy Journal*, **16**(11): 1306-1314.
- Pihlanto, A., 2001. Bioactive peptides derived from bovine whey proteins: opioid and ace-inhibitory peptides. *Trends in Food Science and Technology*, **11**: 347-356.
- Pihlanto, L.A., Rokka T., Korhonen H., 1998. Angiotensin I converting enzyme inhibitory peptides derived from bovine milk proteins. *International Dairy Journal*, **8**: 325-331.
- Plaza, M., Cifuentes, A., and Ibañez, E. 2008. In the search of new functional food ingredients from algae. *Trends in Food Science and Technology*, **19**(1): 31-39.
- Polat, S., and Ozogul, Y. 2009. Fatty acid, mineral and proximate composition of some seaweeds from the northeastern Mediterranean coast. *Italian Journal of Food Science*, **21**(3): 317-324.
- Ponce, N. M. A., Pujol, C. A., Damonte, E. B., Flores, M. L., and Stoerz, C. A. 2003. Fucoidans from the brown seaweed *Adenocystis utricularis*: extraction methods, antiviral activity and structural studies. *Carbohydrate Research*, **338**(1): 153-165.
- Popper, Z.A., Michel, G., Herve, C., Domozych, D.S., Willats, W.G.T., Tuohy, M.G., Kloareg, B., and Stengel, D.B. 2011. Evolution and diversity of plant cell walls: from algae to flowering plants. *Annual Review Plant Biology*, **62**: 567-590.
- Qian, Z. J., Je, J. Y. and Kim, S. K. 2007. Antihypertensive effect of angiotensin I converting enzyme-inhibitory peptide from hydrolysates of Bigeye tuna dark muscle, *Thunnus obesus*. *Journal of Agricultural and Food Chemistry*, **55**(1): 8398-8403.
- Queiroz, K. C. S., Medeiros, V. P., Queiroz, L. S., Abreu, L. R. D., Rocha, H. A. O., Ferreira, C. V., Juca, M.B., Aoyama, H., and Leite, E.L. 2008. Inhibition of reverse transcriptase activity of HIV by polysaccharides of brown algae. *Biomedicine and Pharmacotherapy*, **62**(1): 303-307.
- Rabilloud, T. 1998. Use of thiourea to increase the solubility of membrane proteins in two-dimensional electrophoresis. *Electrophoresis*, **19**: 758-760.
- Rabilloud, T. 2002. Two-dimensional gel electrophoresis in proteomics: Old, old fashioned, but it still climbs up the mountains. *Proteomics*, **2**: 3-10.
- Rabilloud, T., Chevallet, M., Luche, S., and Lelong, C. 2010. Two-dimensional gel electrophoresis in proteomics: Past, present and future. *Journal of Proteomics*, **73**(11): 2064-2077.

- Radmer, R.J. 1996. Algal diversity and commercial algal products. *Bioscience*, **46**(4), 263-270.
- Rajauria, G., Kumar, A., Abu-Ghannam, N., and Gupta, S. 2010. Effect of hydrothermal processing on colour, antioxidant and free radical scavenging capacities of edible Irish brown seaweeds. *International Journal of Food Science and Technology*, **45**(1): 2485-2493.
- Rathore, S. S., Chaudhary, D. R., Ghosh, G. N. B. A., Bhatt, B. P., Zodape, S. T. and Patolia, J. S. 2009. Effect of seaweed extract on the growth, yield and nutrient uptake of soybean (*Glycine max*) under rainfed conditions. *South African Journal of Botany*, **75**(1): 351-355.
- Rehm, B.H.A. 2009. Alginate production: precursor, biosynthesis, polymerization and secretion. *In: Alginates: Biology and Applications* (eds. A. Steinbuchel and B. H. A. Rehm), Springer: Berlin, Germany; pp. 55–72.
- Renaud, S.M., and Luong-Van, J.T. 2006. Seasonal variation in the chemical composition of tropical australian marine macroalgae. *Journal of Applied Phycology*, **18**(3-5): 381-387.
- Rinaudo, M. 2008. *Polyelectrolytes derived from natural polysaccharides*. *In: Monomers, Polymers and Composites from Renewable Resources* (eds. M. N. Belgacem and A. Gandini), Elsevier, Amsterdam: The Netherlands; pp. 495–516.
- Rodrigues, S.P., Ventura, J.A., Zingali, R.B. and Fernandes, R.M.B. 2009. Evaluation of sample preparation methods for the analysis of papaya leaf proteins through two-dimensional gel electrophoresis. *Phytochemical Analysis*, **20**(6): 456-464.
- Rogers, J.V., McDougal, J.N., Price, J.A., Reid, F.M., and Graham, J.S., 2008. Transcriptional responses associated with sulfur mustard and thermal burns in porcine skin. *Cutaneous and Ocular Toxicology*, **27**: 135-160.
- Rose J. K. C., Bashir S., Giovannoni J. J., Jahn M. M., and Saravanan R. S. 2004. Tackling the plant proteome: practical approaches, hurdles and experimental tools. *The Plant Journal*, **39**(1): 715-733.
- Rosegrant, M. W. and Cline, S. A. 2003. Global food security: challenges and policies. *Science*, **302**:1917-1919.
- Ruperez, P. 2002. Mineral content of edible marine seaweeds. *Food Chemistry*, **79**: 23-26.
- Rupérez, P., Ahrazem, O. and Leal, A. J. 2002. Potential antioxidant capacity of sulphated polysaccharides from the edible marine brown seaweed *Fucus vesiculosus*. *Journal of Agricultural and Food Chemistry*, **50**(4): 840-845.



- Rupérez, P., and Saura-Calixto, F. 2001. Dietary fibre and physicochemical properties of edible Spanish seaweeds. *European Food Research and Technology*, **212**(3): 349-354.
- Saad, B., Sing, Y. Y., Nawi, M. A., Hashim, N., Mohamed Ali, A. S., Saleh, M. I., and Ahmad, K. 2007. Determination of synthetic phenolic antioxidants in food items using reversed-phase HPLC. *Food Chemistry*, **105**(1): 389-394.
- Sade, A., Ali, I. and Ariff, M.R.M. 2006. The seaweed industry in Sabah, East Malaysia. *Jati*, **11**(1): 97-107.
- Salekdeh, G.H. and Komatsu, S. 2007. Crop proteomics: aim at sustainable agriculture of tomorrow. *Proteomics*, **7**: 2976-2996.
- Samarakoon, K. and Jeon, Y.J. 2012. Bio-functionalities of proteins derived from marine algae: a review. *Food Research International*, **48**:948-960.
- Samaranayaka, A.G.P., and Li-Chan E.C.Y. 2011. Food-derived peptidic antioxidants: a review of their production, assessment, and potential applications. *Journal of Functional Foods*, **3**(4): 229-254.
- Santoso, J., Yoshie-Stark, Y., and Suzuki, T. 2004. Anti-oxidant activity of methanol extracts from Indonesian seaweeds in an oil emulsion model. *Fisheries Science*, **70**(1): 183-188.
- Saravanan, R.S. and Rose, J.K.C. 2004. A critical evaluation of sample extraction techniques for enhanced proteomic analysis of recalcitrant plant tissues. *Proteomics*, **4**(9): 2522-2532.
- Saritha, K., Mani, A.E., Priyalaxmi, M. and Patterson, J. 2013. Antibacterial activity and biochemical constituents of seaweed *Ulva lactuca*. *Global Journal of Pharmacology*, **7**: 276-282.
- Sartal, C. G., Alonso, M. C. B., and Barrera, P.B. 2011. Application of Seaweeds in the Food Industry. In: *Handbook of Marine Macroalgae: Biotechnology and Applied Phycology*, Edited by Se-Kwon Kim. John Wiley and Sons, Ltd. pp. 522-531.
- Sato, M., Hosokawa, T., Yamaguchi, T., Nakano, T., Muramoto, K., Kahara, T., Funayama, K., Kobayashi, A., and Nakano, T. 2002. Angiotensin I-converting enzyme inhibitory peptides derived from wakame (*Undaria pinnatifida*) and their antihypertensive effects in spontaneously hypertensive rats. *Journal of Agricultural and Food Chemistry*, **50**: 6245-6252.
- Schlimme, E., and Meisel, H. 1995. Bioactive peptides derived from milk proteins. Structural, physiological, and analytical aspects. *Die Nahrung*, **39**: 1-20.

- Scholten, A., Poh, M.K., VanVeen, T.A., VanBreukelen, B., Vos, M.A., and Heck, A.J. 2006. Analysis of the cGMP/cAMP interactome using a chemical proteomics approach in mammalian heart tissue validates sphingosine kinase type 1-interacting protein as a genuine and highly abundant AKAP. *Journal of Proteome Research*, **5**(6): 1435-1447.
- Schrader, M., and Schulz-Knappe, P. 2001. Peptidomics technologies for human body fluids. *Trends in Biotechnology*, **19**: 55-60.
- Schrattenholz, A. and Groebe, K. 2007. What does it need to be a biomarker? Relationships between resolution, differential quantification and statistical validation of protein surrogate biomarkers. *Electrophoresis*, **28**(12): 1970-1979.
- Schuster A.M., and Davies E. 1983. Ribonucleic acid and protein metabolism in pea epicotyls. II. Response to wounding in aged tissue. *Plant Physiology*, **73**(1): 817-821.
- Seager, S.L., and Slabaugh M.R. 2014. *Chemistry for Today: General, Organic, and Biochemistry*, 8th Edition, Brooks/Cole, Cengage Learning. USA. pp. 624-625.
- Senechal, S. and Kussmann, M. 2011. Nutriproteomics: technologies and applications for identification and quantification of biomarkers and ingredients. *Proceedings of the Nutrition Society*, **70**(1): 351-364.
- Seol, K. H., Lim, D. G., Jang, A., Jo, C., and Lee, M. 2009. Antimicrobial effect of κ-carrageenan-based edible film containing ovotransferrin in fresh chicken breast stored at 5 °C. *Meat Science*, **83**(1): 479-483.
- Shahidi, F., and Zhong, Y. 2008. Bioactive peptides. *Journal AOAC International*, **9**(4): 914-931.
- Shanmugam, M., and Mody, K. H. 2000. Heparinoid-active sulphated polysaccharides from marine algae as potential blood anticoagulant agents. *Current Science*, **79**(1): 1672-1683.
- Sharma, S., Singh, R. and Rana, S. 2012. Prediction of Structures of Bioactive Peptides by Using Homology Approach. *International Journal of Drug Formulation and Research*, **3**(1): 69-80.
- Shen, Y., Tolic, N., Liu, T., Zhao, R., Petritis, B.O., Gritsenko, M.A., Camp, D.G., Moore, R.J., Purvine, S.O., Esteva, F.J., and Smith, R.D. 2010. Blood peptidome-degradome profile of breast cancer. *PLoS One*, **5**(10), e13133.
- Shiu, C. T., and Lee, T. M. 2005. Ultraviolet-B-induced oxidative stress and responses of the ascorbate–glutathione cycle in a marine macroalga *Ulva fasciata*. *Journal of Experimental Botany*, **56**: 2851-2865.

- Siah, W.M., Aminah, A., and Ishak, A. 2015. Edible films from seaweed (*Kappaphycus alvarezii*). *International Food Research Journal*, **22**(6): 2230-2236.
- Sieber, R., Butikofer, U., Egger, C., Portmann, R., Walther, B., and Wechsler, D. 2010. ACE-inhibitory activity and ACE inhibiting peptides in different cheese varieties. *Dairy Science Technology*, **90**: 47-73.
- Siemensma, A.D., Weijer, W.F.I., and Bak, H.J. 1993. The importance of peptide lengths in hypoallergenic infant formula. *Trends in Food Science and Technology*, **4**: 16-21.
- Silva, L. M. C. M., Lima, V., Holanda, M. L., Pinheiro, P. G., Rodrigues, J. A. G., Lima, M. E. P., Benevides, N. M. B. 2010. Antinociceptive and anti-inflammatory activities of lectin from marine red alga *Pterocladia capillacea*. *Biological and Pharmaceutical Bulletin*, **33**: 830-835.
- Silva, T. M. A., Alves, L.G., DeQueiroz, K. C. S., Santos, M. G. L., Marques, C. T., Chavante, S. F., Rocha, H.A., and Leite, E.L. 2005. Partial characterization and anticoagulant activity of a heterofucan from the brown seaweed *Padina gymnospora*. *Brazilian Journal of Medical and Biological Research*, **38**(1): 523-533.
- Sirtori, C.R., Galli, C. Anderson, J.W., and Arnoldi, A. 2009. Nutritional and nutraceutical approaches to dyslipidemia and atherosclerosis prevention: Focus on dietary proteins. *Atherosclerosis*, **203**: 8-17.
- Skolnick, J., and Fetrow, J.S. 2000. From genes to protein, structure and function: Novel applications of computational approaches in the genomic era. *Trends in Biotechnology*, **18**: 34-39.
- Smit, A. J. 2004. Medicinal and pharmaceutical uses of seaweed natural products: A review. *Journal of Applied Phycology*, **16**(1): 245-262.
- Song, K. C., Lee, H. S., Choung, I. Y., Cho, K. I., Ahn, Y., and Choi, E. J. 2006. The effect of type of organic phase solvents on the particle size of poly (D, L-lactide-co-glycolide) nanoparticles. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, **276**(3): 162-167.
- Song, Y., Liu, L., Shen, X., You, J., and Luo, K. 2011. Effect of sodium alginate-based edible coating containing different anti-oxidants on quality and shelf life of refrigerated bream (*Megalobrama amblycephala*). *Food Control*, **22**(1): 608-615.
- Soni, B., Visavadiya, N.P., and Madamwar, D. 2009. Attenuation of diabetic complications by C-phycoerythrin in rats: antioxidant activity of C-phycoerythrin including copper-induced lipoprotein and serum oxidation. *British Journal of Nutrition*, **102**: 102-109.

- Spolaore, P., Joannis-Cassan, C., Duran, E., and Isambert, A. 2006. Commercial applications of microalgae. *Journal of Bioscience and Bioengineering*, **101**: 87-96.
- Stengel, D. B., Connan, S., and Popper, Z. A. 2011. Algal chemodiversity and bioactivity: Sources of natural variability and implications for commercial application. *Biotechnology Advances*, **29**(5): 483-501.
- Suetsuna, K. 1998. Purification and identification of angiotensin I-converting enzyme inhibitors from the red alga *Porphyra yezoensis*. *Journal of Marine Biotechnology*, **6**: 163-167.
- Suetsuna, K. and Nakano, T. 2000. Identification of an antihypertensive peptide from peptic digest of wakame (*Undaria pinnatifida*). *Journal of Nutritional Biochemistry*, **11**(1): 450-454.
- Sugiura, Y., Matsuda, K., Yamada, Y., Nishikawa, M., Shioya, K., Katsuzaki, H., Imai and Amano. 2006. Isolation of a new anti-allergic phlorotannin, phlorofucofuroeckol-B, from an edible brown alga, *Eisenia Arborea*. *Bioscience, Biotechnology, and Biochemistry*, **70**: 2807-2811.
- Tabarsa, M., Rezaei, M., Ramezanpour, Z., and Waaland, J. R. 2012. Chemical compositions of the marine algae *Gracilaria salicornia* (Rhodophyta) and *Ulva lactuca* (Chlorophyta) as a potential food source. *Journal of the Science of Food and Agriculture*, **92**(2): 2500-2506.
- Tan, S.P., Sullivan, L.O., Prieto, M.L., Mcloughlin, P., Lawlor, P.G., Hughes, H., and Gardiner, G.E. 2014. Seaweed antimicrobials: isolation, characterization, and potential use in functional foods. *Bioactive Compounds from Marine Foods: Plant and Animal Sources*, First Edition. John Wiley and Sons, Ltd. pp. 269-312.
- Tan, Y.N., Ayob, M.K., and Wan Yaacob, W.A., 2013. Purification and characterisation of antibacterial peptide-containing compound derived from palm kernel cake. *Food Chemistry*, **136**: 279-284.
- Teng, D., Fang, Y., Song, X., and Gao, Y. 2011. Optimization of enzymatic hydrolysis parameters for antioxidant capacity of peptide from goat placenta. *Food and Bioproducts Processing*, **89**: 202-208.
- Thapa, B.R. 2005. Therapeutic potentials of bovine colostrums. *Indian Journal of Paediatrics*, **72**(1): 849-852.
- Thelen, J.J., and Peck, S.C. 2007. Quantitative proteomics in plants: choices in abundance. *Plant Cell*, **19**: 3339-3346.
- Thiellement, H., Bahrman, N., Damerval, C., Plomion, C., Rossignol, M., Santoni, V., de Vienne, D., and Zivy, M. 1999. Proteomics for genetic and physiological studies in plants. *Electrophoresis*, **20**: 2013-2026.

- Thiellement, H., Zivy, M. and Plomion, C. 2002. Combining proteomic and genetic studies in plants. *Journal of Chromatography B*, **782**: 137-149.
- Thirumaran, G., and Anantharaman, P. 2009. Daily growth rate of field farming Seaweed *Kappaphycus alvarezii* (Doty) Doty ex P. Silva in Vellare estuary. *World Journal of Fish and Marine Sciences*, **1**: 144-153.
- Thomä-Worringer, C., Sörensen, J. and López-Fandino, R. 2006. Health effects and technological features of caseinomacro-peptide. *International Dairy Journal*, **16**: 1324-1333.
- Tripathi, V. and Vashishtha, B. 2006. Bioactive compounds of colostrum and its application. *Food Reviews International*, **22**: 225-244.
- Turkmen, N., Sari, F., and Velioglu, Y. S. 2005. The Effect of Cooking Methods on Total Phenolics and Antioxidant Activity of Selected Green Vegetables. *Food Chemistry*, **93**(4): 713-718.
- Turner, N. J. 2003. The ethnobotany of edible seaweed (*Porphyra abbottae* and related species: *Rhodophyta bangiales*) and its use by first nations on the Pacific Coast of Canada. *Canadian Journal of Botanic*, **81**: 283-293.
- Udenigwe, C.C., and Aluko, R.E. 2012. Food protein-derived bioactive peptides: Production, processing and potential health benefits. *Journal of Food Science*, **77**:11-24.
- USDA, 2001. Agricultural Research Service. Nutrient Database for Standard Reference, Release 14.
- Venugopal, V. 2011. *Polysaccharides from Seaweed and Microalgae Marine Polysaccharides Food Applications*. Boca Raton, USA: CRC Press. pp.89-129.
- Vercauteren, F.G., Arckens, L. and Quirion, R. 2007. Applications and current challenges of proteomic approaches, focusing on two-dimensional electrophoresis. *Amino Acids*, **33**(3): 405-414.
- Verlaque, M., Durand, C., Huisman, J.M., Boudouresque, C.F., Le Parco, Y., 2003. On the identity and origin of the Mediterranean invasive *Caulerpa racemosa* (Caulerpaceae, Chlorophyta). *European Journal of Phycology*, **38**: 325-339.
- Vilhelmsson, O.T., Martin, S.M., Poli, B. M., and Houlihan, D.F. 2007. Proteomics: Methodology and Application in Fish Processing. *Food Biochemistry and Food Processing*, **43**:401-422.
- Vincent, D., Wheatley, M.D. and Cramer, G.R. 2006. Optimization of protein extraction and solubilization for mature grape berry clusters. *Electrophoresis*, **27**(9): 1853-1865.

- Viskari, P.J., and Colyer, C.L. 2003. Rapid extraction of phycobiliproteins from cultures cyanobacteria samples. *Analytical Biochemistry*, **319**: 263-271.
- Vitzthum, F., Behrens, F., Anderson, N.L., and Shaw, J.H. 2005. Proteomics: From basic research to diagnostic application. A review of requirements and needs. *Journal of Proteome Research*, **4**(4):1086-1097.
- Vorob'ev, M.M., and Goncharova, A. 1998. Computer simulation of proteolysis. Peptic hydrolysis of partially demasked  $\beta$ -lactoglobulin. *Nahrung*, **2**: 61-67.
- Vuorelaa, P., Leinonenb, M., Saikkuc, P., Tammela, P., Rauhad, J.P., Wennberge, T. and Vuorela, H. 2004. Natural products in the process of finding new drug candidates. *Current Medicinal Chemistry*, **11**(1): 1375-1389.
- Waldmann, H. 2003. At the Crossroads of Chemistry and Biology. *Bioorganic and Medicinal Chemistry*, **11**: 3045-3051.
- Wang, T., Jonsdottir, R., Kristinsson, H. G., Hreggvidsson, G. O., Jonsson, J. O., Thorkelsson, G., and Olafsdottir, G. 2010. Enzyme-enhanced extraction of antioxidant ingredients from red algae *Palmaria palmata*. *LWT- Food Science and Technology*, **43**: 1387-1393.
- Wang, W., and De Mejia, E.D. 2005. A new frontier in soy bioactive peptides that may prevent age-related chronic diseases. *Comprehensive Reviews in Food Science and Food Safety*, **4**: 63-78.
- Wang, W., Scali, M., Vignani, R., Spadafora, A., Sensi, E., Mazzuca, S. and Cresti, M. 2003. Protein extraction for two-dimensional electrophoresis from olive leaf, a plant tissue containing high levels of interfering compounds. *Electrophoresis*, **24**(14): 2369-2375.
- Wang, W., Vignani, R., and Cresti, M.S.M. 2006. A universal and rapid protocol for protein extraction from recalcitrant plant tissues for proteomic analysis. *Electrophoresis*, **27**: 2782-2786.
- Wang, Y., You, J., Yu, Y., Qu, C., Zhang, H., Ding, L., Zhang, H., and Li, X. 2008. Analysis of ginsenosides in *Panax ginseng* in high pressure microwave-assisted extraction. *Food Chemistry*, **110**(1): 161-167.
- Washburn, M.P., Wolters, D., Yates, J.R. III. 2001. Large-scale analysis of the proteome by multidimensional protein identification technology. *Nature Biotechnology*, **19**: 242-247.
- Watson, B.S., Asirvatham, V.S., Wang, L., and Sumner, L.W. 2003. Mapping the proteome of barrel medic (*Medicago truncatula*). *Plant Physiology*, **131**: 1104-1123.

- Weiss, W., and Gorg, A. 2008. Sample solubilization buffers for two-dimensional electrophoresis. *In: Methods in Molecular Biology-2D PAGE: Sample Preparation and Fractionation*. Ed.: Posch, A. Humana Press, Totowa NJ, pp. 35-42.
- Westermeier, R. 2005 *Electrophoresis in practice*. 4th edition. Wiley-VCH Verlag GmbH and Co. KGaA, Weinheim. pp. 204-205.
- Westermeier, R. 2006. Sensitive, quantitative, and fast modifications for Coomassie Blue staining of polyacrylamide gels. *Proteomics*, **2**: 61-64.
- Westermeier, R. and Naven, T. 2002. *Proteomics in Practice: A Laboratory Manual of Proteome Analysis*. Wiley-Vch, Weinheim, pp. 233-238.
- Wijesekara, I., Pangestuti, R., and Kim, S. K. 2011. Biological activities and potential health benefits of sulfated polysaccharides derived from marine algae. *Carbohydrate Polymers*, **84**(1): 14-21.
- Wijesekara, I., Yoon, N.Y., and Kim, S.K. 2010. Phlorotannins from *Ecklonia cava* (Phaeophyceae): biological activities and potential health benefits. *BioFactors*, **36**: 408-414.
- Wikfors, G. H. and Ohno, M. 2001. Impact of algal research in aquaculture. *Journal of Phycology*, **37**(1): 968-974.
- Wilkins, M.R., Gasteiger, E., Sanchez, J.C., Bairoch, A., and Hochstrasser, D.F. 1998. Two-dimensional Gel electrophoresis for proteome projects: the effects of protein hydrophobicity and copy number. *Electrophoresis*, **19**: 1501-1505.
- Wilkins, M.R., Sanchez, J.C. Andrew, A. G., Ron D.A., Ian, H.S., Denis, F. H. and Keith, L. W. 1996. Progress with proteome projects: why all proteins expressed by a genome should be identified and how to do it. *Biotechnology and Genetic Engineering Reviews*, **13**(1):19-50,
- Williams, T. L., Leopold, P. and Musser, S. 2002. Automated post processing of electrospray LC/MS data for profiling protein expression in bacteria. *Analytical Chemistry*, **74**(1): 5807-5813.
- Wong, K.H. and Cheung, P.C.K. 2000. Nutritional evaluation of some subtropical red and green seaweeds - Part I - proximate composition, amino acid profiles and some physico-chemical properties. *Food Chemistry*, **71**(1): 475-482.
- Wong, P.F., Tan, L.J., Nawi, H. and Abu Bakar, S. 2006. Proteomics of the red alga, *Gracilaria changii* (Gracilariales, Rhodophyta). *Journal of Phycology*, **42**(1):113-120.
- Wu, X., Gong, F., and Wang, W. 2014. Protein extraction from plant tissues for 2DE and its application in proteomic analysis. *Proteomics*, **14**(6): 645-658.

- Xi, J., Wang, X., Li, S., Zhou, X., Yue, L., Fan, J. and Hao, D. 2006. Polyethylene glycol fractionation improved detection of low abundant proteins by two-dimensional electrophoresis analysis of plant proteome. *Phytochemistry*, **67**: 2341-2348.
- Xie, Z., J. Huang, X. Xu, and Z. Jin, 2008. Antioxidant activity of peptides isolated from alfalfa leaf protein hydrolysate. *Food Chemistry*, **111**(2): 370-376.
- Yao, Y., Vuong, C., Kocianova, S., Villaruz, A.E., Lai, Y., Sturdevant, D.E., and Otto, M. 2006. Characterization of the *Staphylococcus epidermidis* accessory-gene regulator response: quorum-sensing regulation of resistance to human innate host defense. *The Journal of Infectious Diseases*, **193**: 841-848.
- Yates, J. R. 1998. Mass Spectrometry and the Age of the Proteome. *Journal of Mass Spectrometry*, **33**(1): 1-19.
- Ye, H., Wang, K., Zhou, C., Liu, J., and Zeng, X. 2008. Purification, Antitumor and Antioxidant Activities *in Vitro* of Polysaccharides from the Brown Seaweed *Sargassum pallidum*. *Food Chemistry*, **111**(2): 428-432.
- Yoon, N.Y., Kim, H.R., Chung, H.Y., and Choi, J.S. 2008. Anti-hyperlipidemic effect of an edible brown algae, *Ecklonia stolonifera*, and its constituents on poloxamer 407-induced hyperlipidemia and cholesterol-fed rats. *Archives of Pharmacal Research*, **31**(1): 1564-1571.
- Yoshie, Y., Wand, W., Hsieh, Y. P., and Suzuki, T. 2002. Compositional difference of phenolic compounds between two seaweeds, *Halimeda* spp. *Journal of the Tokyo University of Fisheries*, **88**: 21-24.
- YoshieStark, Y., Wada, Y. Schott, M., and Wäsche, A. 2006. Functional and bioactive properties of rapeseed protein concentrates and sensory analysis of food application with rapeseed protein concentrates. *LWT-Food Science and Technology*, **39**(5): 503-512.
- Yotsukura, N. 2010. Production of kelp in Japan: various natural resources and the established aquaculture technique. *Seaweeds for Human Consumption, Bioactive Compounds, and Combating of Diseases: An international interdisciplinary symposium*, Carlsberg Academy, Copenhagen, August 26-27, 2010.
- Yotsukura, N., Nagai, K., Kimura, H., and Morimoto, K. 2009. Seasonal changes in proteomic profiles of Japanese kelp: *Saccharina japonica* (Laminariales, Phaeophyceae). *Journal of Applied Phycology*, **22**(4): 443-451.
- Yotsukura, N., Nagai, K., Tanaka, T., Kimura, H. and Morimoto, K. 2012. Temperature stress-induced changes in the proteomic profiles of *Ecklonia cava* (Laminariales, Phaeophyceae). *Journal of Applied Phycology*, **24**: 163-171.



- Zhang, Y., Fonslow, B.R., Shan, B., Baek, M.C., and Yates, J.R. III 2013. Protein analysis by shotgun/bottom-up proteomics. *Chemical Reviews*, **113**(4): 2343-2394.
- Zhang, Y.M., Zhao, J.M., Xiang, Y., Bian, X.C., Zuo, Q.M., Shen, Q., Gai, J.Y. and Xing, H. 2011. Proteomics study of changes in soybean lines resistant and sensitive to *Phytophthora soja*. *Proteome Science*, **9**: 52-59.
- Zou, Y., Qian, Z.-J., Li, Y., Kim, M.-M., Lee, S.-H., and Kim, S.-K. 2008. Antioxidant effects of phlorotannins isolated from *Ishige okamuraein* free radical mediated oxidative systems. *Journal of Agricultural and Food Chemistry*, **56**(16): 7001-7009.
- Zubia, M., Fabre, M.S., Kerjean, V., Le Lann, K., Stiger-Pouvreau, V., Fauchon, M., and Deslandes, E. 2009. Antioxidant and antitumoural activities of some Phaeophyta from Brittany coasts. *Food Chemistry*, **116**(1): 693-701.
- Zubia, M., Payri, C. and Deslandes, E. 2008. Alginate, mannitol, phenolic compounds and biological activities of two range-extending brown algae, *Sargassum mangarevense* and *Turbinaria ornate* (Phaeophyta: Fucales), from Tahiti (French Polynesia). *Journal of Applied Phycology*, **20**: 1033-1043.