The global challenges and compliance in outsourcing compatible tangible bioactive compounds from local geochemical signatures marine organisms

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Abstract. There a new perspective in tangible bioactive metabolites and drug outsourcing from indigenous marine organisms and its related sustainable commercial and industrial-able pharmacological efficacies screening and discovery. In pertinent as *Halal Thoyyiban* evidence marine based products, these bioactive metabolites extracted from selected anatomical region of the organisms biomass was extrapolated and a transformation brought by studying much purported indigenous folk and traditional medicine practices in these millennia. This research paper discusses the potential imminent issues and challenges of outsourcing compatible tangible bioactive compounds from local geochemical signatures marine organisms in a novel fulfillment effort during the global and Malaysia millennia fourth industrial revolution era, of compliance as *Halal Thoyyiban* bioactive compounds and in compliance with related Islamic legal issues. *Vis a Vis* the paper covers challenges perspectives such as; adulteration, dilemma in wild stock prevalence study, community awareness, market competitiveness and supply chain management from our innovative research products. It elaborates on each to bolsters and provides the essential information for optimized sustainable commercial exploitation in future research and outsourcing activities from indigenous geochemical signature marine organisms that can provide solutions to such issues: outsourcing and industrial dilemma in compliance of Halal *Thoyyiban* agenda.

Introduction

Folklore plant fauna and its extracts have indeed bequeathed geographically to influenced local medicine and the design of cultural landscape that they are still part of from generation to generation. As such have help provided in these millennia biotechnological drug discovery that rhetorically have been well purported in ancient believe that is rich in domestic recipes and communal practice. As such plant fauna-derived extracts are valuable tangible sources in folk-medicine practiced by 80% of the world population to treat a wide range of disease conditions, including microbial, larvicidal and inflammatory infections (Kinghorn *et al.*, 2011; Newman and Cragg, 2012). The state of world marine stocks has mostly been confined to assessing the impacts of fishing. Studies have estimated that 75% of world fisheries are fully exploited, of which 28% are in the state of over-fishing. The inability to continue to increase the catch of marine species and a large percentage of fisheries that are fully exploited are interpreted by some to indicate that there is a crisis in the world marine fisheries. In this millennia, marine based products especially in pertinent to bioactive metabolites and biocompounds have now created a strong presence in international trade as a tangible commercial-able outsource biomass. However there are imminent issues and challenges of outsourcing compatible tangible bioactive compounds from geochemical signatures marine organisms in a novel fulfilment effort during the millennia fourth industrial era, including bioactive compounds that are of compliance to Halal Thoyyiban concept and other related Islamic legal issues. *Vis a Vis* the challenges cover perspectives such as; adulteration, wild stock prevalence study dilemma, community awareness, market competitiveness and supply chain management. The significant is to elaborates, bolsters and provides the essential information for optimized sustainable commercial exploitation that complies with Islamic legal issues and subsequently provides solutions to issues in future research.

The challenges and its perspectives

The first challenge: religious, social issues and good manufacturing practices.

Globally, throughout the long trajectory of evolution, humans have learned to optimise and utilized marine fisheries; flora and fauna signatures as functional food and as efficacies for treatments of communal ailments as widely purported in folk and traditional medicine history. Pertaining to the Muslim *ummah,* the halal bioactive compounds and the Islamic legal issues arise from the absence of a standard definition of halal, which has led to differences in the degree of acceptance in different countries. In some countries, halal requirements are confined to the prohibition of porcine and alcohol-based products that are clearly stipulated in the Quran. In tandem to this, in other countries, the halal standard's requirement includes suitability of its manufacturing tools, build-up components of its raw materials and critical path of its adapted multi process. Differences in opinion and specifications also relate to filthy ingredients, including exerbating pus from the clinical sores of diseased animals, horse and calf serum, urine and macerated cancerous cells. The manufacturing

of marine bioactive compounds is a complicated process that poses major challenges to the local industry. Most marine organisms and its tissues easily eviscerated and die off upon separation from the seawater. Moreover, a longer time is needed especially for small scale entrepreneur to develop, optimize, pattern and commercialize a new commercial exploitable bioactive compound. Production is subjected to stringent regulatory requirements such as the setting up of a standardized syariah-compliant facility that may, in some cases, very costly. Additional costs are also incurred in logistics, as halal bioactive compounds will need to be transported separately from possible accompanied non-halal products. Sadly the knowledge pathway also highlights shortage of trained experts to properly voucher well-defined taxonomy of marine organisms and a capable of auditing (the halal manufacturing process from local geochemical signatures marine flora and fauna. In pertinent to social issues such as safety, cleanliness, nutritious, quality, authentication of the marine based biocompounds or products, always been questioned and sometimes ultra vies. As this communal way of lifestyle issues is itself a dilemma that have been adapted from local geographical believe, which are mostly with poor hygienic practice and ill-defined without any relevant non-scientific evidence folk medicine practices.

The second challenge: recognition of marine organism's biomass scientific tangibilities and dilemma.

In these millennia, 2 billion Muslim populations are expected by 2020, while other research scholars have indicate that growth of Muslim population is expected to increase from 1.8 billion in 2015 to 3.0 billion in 2060 (Lipka & Hackett, 2017). This expectation signifies a growth rate of 1.5% annually, and Malaysia will continue to give Halal Thoyyiban sector a special focus to help boost its economic growth. The industrial fourth revolution present challenges and opportunities in the halal industry and will create blue ocean transformation for the global Halal market. The ocean is the tangible source of structurally unique marine natural products. These exploitable marine based natural products are believed to be mainly accumulated in most local iconic geochemical signatures invertebrates' biomass such as the echinoderm, sponges, tunicates, bryozoans, and molluscs. These marine invertebrates and organisms have developed highly specific relationships with numerous intertidal associated microorganisms and their ecosystem. As such there are species that are sand / sediment feeder, predators and coral friendly intertidal animals. In this millennium, many marine invertebrates based products that have anticancer, antimicrobial and anti-inflammatory [Sonnenschein, *et al.,* 2004]. As such stocking marine areas in developing fisheries oriented countries present special challenges and opportunities. Whereas in many developed countries fishing is viewed as a romantic profession to be maintained, and as the basic right of the population, in developing countries it is often the employment of the last resort. The bioactive compounds are harvest biotechnologically from the marine intertidal fisheries flora and fauna. As such better exchange of information on contemporary research findings and valuable current high-tier inputs in improving existing policies, strategies, and an implementable action plan are continuously needed and mitigate able to further develop Halal Thoyyiban Industry that conforms to the Islamic teachings or facilitates the practice of the religion [Henderson, 2016). The life histories, reproductive capabilities and feeding of many of these marine intertidal fisheries flora and fauna is complex, tagging is almost difficult [as comparison to inland animals although such practice not a recommended practice in compliance to halal status of the said inland animals], while restocking and stock enhancement programs to reduce dependent to wild stock have yet to be systematically designed so that released juveniles can complete their life cycle and thus contribute to spawning biomass. More ever feeding and dilemma to coastal nutrient outpouring from reverine animal husbandry urbanisation, from catastrophic episodes like flood can add factors for cross-examine and to elucidation the dilemma either or not have bid and in compliance to Islamic regulation. Thus to enhance marine base product into the global market, research process and development will need to obtain new knowledge and use that knowledge to ensure compliance and improve accreditation procedures. As such, large scientific based evidences investments in a multi-disciplinary team are holistically needed to elucidate all the important components of marine live and organisms' complex life history and develop technology for releases at a meaningful scale in a responsible way. As such, in pertinent to Halal Thoyyiban to this marine agenda, there should be synergies created between Thoyyiban practice of sustainable commercial exploitation of geochemical signatures harvested bioactive compound, Islamic principle practices aquaculture and knowledge equipped awareness of coastal fisheries to help meet the future demand for its much sourced biomass and aid in restoring depleted wild stocks.

In an innovative tailor design study to investigate the effect of total sulfated glycosaminoglycan (GAG) from integument body wall of sea cucumber *Stichopus vastus* on inflammatory mediators and tissue healing on rodents with full thickness burn injury. Sea cucumbers, also known as Gamat in Malay are marine invertebrates from the phylum Echinodermata (Kamarul, *et al.,* 2010) and can be found throughout the worlds' ocean intertidal beds (Fredalina, *et al.,* 1999). Throughout the world there are more than 2500 sea cucumbers species (Ibrahim. 2003). Among the most popular species are *Stichopus hermanni, Stichopus vastus, Stichopus badionotus, Stichopus chloronotus, Holothuria atra, Holothuria edulis, and Holothuria scabra* (Ridzwan, *et al.,* 1995). In one of our study (Mohd Faeiz Pauzi, *et al*., 2017), twelve male Sprague-dawley rats weighting 350-400 grams were distributed randomly into two groups. Six rats in group A received 5 mL/kg/day intra-peritoneal total sulfated GAG from *S*. vastus for 5 days, while control group received phosphate buffered saline (PBS). Level of IL-10 and IL-12 were measured at day 1, 6 and 12. The level of IL-10 revealed significantly ($p<0.05$) higher and the level of IL-12 was reduced significantly ($p<0.05$) in sulfated GAG treated group. Data suggested that sulfated GAG from *S.* vastus integument body wall increase anti-inflammatory cytokine and reduce pro-inflammatory cytokine. Microscopic evaluation showed reduced neutrophils infiltration with enhanced proliferation of fibroblasts and

angiogenesis ($p<0.05$) in the sulfated GAG treated group. Thus sulfated GAG from *S.* vastus integument body wall has impact on the outcome of wound healing process by increasing the level of anti-inflammatory cytokine, the IL-10, and reduced level of pro-inflammatory cytokine, the IL-12 and gave positive effect on fibroblast proliferation and angiogenesis process. The beneficial findings from this study can act as advancement in the field of wound healing by the usage of Malaysian natural products, from the local sea cucumber species.

The outbreak of mad cow disease and foot-and-mouth disease as well as religious restrictions have resulted in rising concerns regarding bovine and porcine collagen as a potential transmitting pathogenic vector of these diseases [Zhang, *et al.,* 2007]. Local geochemical signatures *Acanthaster planci* Crown of Thorns: COTs integumental biomass and its internal tissue were inspected and were found to contained mutable collagen when examined under optical and electron microscopes [Nur Hanim Zainudin, *et al*., 2012, and Nur Afiqah Bahrom, *et al*., 2012]. In echinoderms like Acansther planci, cellular immune responses are carried out by circulating cells, coelomocytes, in their coelomic cavities. In tandem to this, our study has successfully extracted collagen from the body wall of local coral reef associated *Acanthaster planci*: COTs. Pepsin-solubilized collagen (PSC) was isolated from the inert body wall of COTs using pepsin digestion in 0.5 M acetic acid (conventional method). The electrophoretic pattern of PSC showed that it contained two main α- chains components (α1 and α2 chains), suggesting that it might be type I collagen. While the amino acid composition analysis showed that the said PSC contained high content of glycine, proline and hydroxyproline. Fourier transform infrared spectroscopy (FTIR) investigation revealed the existence of triple helix structure of the isolated collagen. Therefore the presence of collagen from local *Acansther planci* COTs seems to support the availability of tangible sulfated polysaccharides representatives' bioactive compound for global medical therapeutic needs (Farid, 2015 and Tan, *et al.,* 2013). The potential and exploitable able biomass was extracted via critical step and dual purposes objectives to exploit GAG from predatory invertebrate and to help safe coral deforestation.

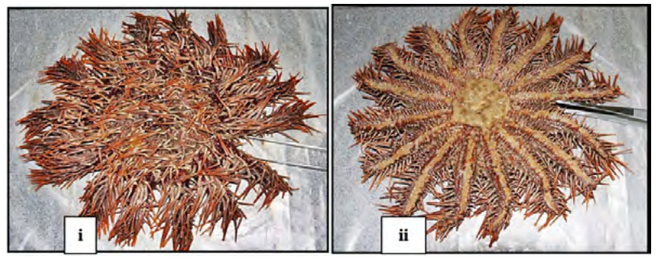

Figure 1: A digital photograph topographical representation of the aboral surface (i) and oral surface (ii) of an adult *Acanthaster planci* crown-of-thorns starfish.

Nanoscience and nanotechnology entail comprehensive understanding and allow modification/manipulation of materials at the atomic, molecular and macromolecular scales. The extraction of marine peptides and proteins of interest from their natural source is usually made in water or aqueous buffers in order to maintain their functionality. Fractionation is often done using a salt (e.g. ammonium sulfate) or acetone. The purification steps usually include chromatographic methods like gel filtration, ion exchange and reverse-phase high performance liquid chromatography (RP-HPLC). This last being the method of choice for the purification of peptides from their natural sources [Conlon, 2007]. While derivatives materials, such as gelatine, sodium stearoyl lactylate, collagen, calcium stearate, capric acid, myristic acid, oleic acid and bone ash are pre-treatment solution/substances, optimize components and products in biotechnological formulation and fabrication for drug discovery and therapeutic bioactive substances. Polymerase chain reaction (PCR) with restriction fragment length polymorphisms (RFLP) analysis of a conserved region in the mitochondrial (mt) cytochrome b (cyt b) gene has been purported and said developed for halal detection (Aida, *et al*., 2005). Although FTIR can be used, to differentiate lard in a mixture of animal fats (lamb, cow and chicken) at selected infrared fingerprint range of 1500-900 cm^{-1} (Rohman & Che Man, 2010) and differentiate mixtures of plant oils such as VCO, palm and olive oil in the frequency regions of 1,120-1,105 and 965-960 cm^{-1}(Rohman, *et al.,* 2010), little is known on FTIR and PCR-based technique of differentiating and characterize halal Thoyyiban products from marine exploitable biomass. As such efforts to harmonization, bio-contemplate to Islamic regulations and ensure the modern biotechnological application approaches prowess enhancement of innovative products [especially from marine base science and animals] balance should be properly strategies and well mitigated in this industrial era. Such harmonisation and mitigation will create knowledge establishment, knowledge accumulation, knowledge maintenance, and knowledge exploitation,

Hidden substances or adulteration of processing ingredients from various sources cause serious problem and dilemma (Riaz and Chaudry, 2003). In these millennia, high need and demand for Shariah binding transparency in processing, biotechnological steps, digestion of pertinent to the Halal Thoyyiban agenda will help to enhance the development of methods for the analysis. Several biotechnological techniques developed such as FTIR, High Performance Liquid Chromatography (HPLC), molecular technique are now available but Halal Thoyyiban authentication and accreditation

must be verse to handle / use it and able to then ensure the '*Suci'* of the said machines is still in place for future activities or detection.

Insight factor for considerations

1. Focuses on delivering a hygienic and healthy marine based innovative products

Research innovations and developments play an important factor that could impact significantly on the future of the Halal Thoyyiban market trends. Research and development is needed by the Halal Thoyyiban institution to trace any haram substances possibly adulterated in marine base products. In pertinent to the forth revolution era agenda on marine based bioactive products. *Per se,* although JAKIM has developed a traceability system that included guidelines for the preparation and handling of halal food industry including nutrient supplements, research innovations and developments products from marine based bioactives do not necessarily are fabricated or prototyped in Halal laboratory institutions. Thus among the enhancement and mitigation strategies to reconsider and enforced, SIRIM (2013), MS1900:2014 is developed based on ISO 9001: 2008. The main idea of MS1900:2014 is to assist organization to deliver products and services, meeting customers' requirements, compliance to regulatory requirements and comply with the *Shariah* requirements. In addition to that, MS1900:2014 inculcate and put into practice the Islamic values system into the organization daily operations. There are three principles behind MS1900:2014. Organization shall strictly adhere to the principles of *halal* and *hara*m as well as the principles of *Muamalat*. The implementation of MS1900:2014 also ensure organization operates based on the "objective of *Shariah* (Maqasid Al-Shariah)". One of the requirements stated in the standard is compliance to *Shariah* requirements in financial management, human resources management, procurement procedures, production and marketing. Under the Islamic values, the concept of Halal Thoyyiban issues covers throughout the whole production process, from raw materials sourcing and purchasing to the consumption of products, where consumers are the utmost driver to the growth of marine based industry. In order to assure the consistency of quality standard and guidelines, there are over 200 different halal certifications globally. As such companies awarded with halal certification/logo are given a trust on the authenticity of Halal to carry the responsibility of delivering a hygienic and healthy products and services in accordance with Islamic guidelines (Aliff, *et al*., 2015, Zailani, *et al.,* 2010). Apart from that, the additional key authenticity prowess certification may be needed to be pursued. For example, for pharmaceutical authenticity Chemistry Departments and National Pharmaceutical Regulatory Agency (NPRA) might also be a tangible involvement. Other certification process will include such as Good Manufacturing Practices (GMP) and Hazard Analysis and Critical Control Point (HACCP).

2. Focuses on the religious dimensions and values.

Marine based products especially in pertinent to bioactive metabolites and biocompounds have created a strong presence in international trade. And halal markets are the fast growing economies of the Asia, Middle East, Europe and the Americas. To revolutionized the global food industry and although halal food hub/park have been extrapolated, to optimum the Malaysia industrial revolution era in this millennia, especially of pertinent to leveraging halal marine based products and ecosystem, a national Halal heritage trust/foundation/centre of excellence is proposed to bolster the overall halal ecosystem and segments by: 1. Pioneering Halal Thoyyiban certification not just as a brand but as a way of life and a well acknowledged Islam accredited paten, and 2. Ensure wide availability and selection of halal food throughout the country and 3. Educated and transform local communities' great understanding of Halal Thoyyiban products and its Muslim community catchphrase of choice for the when dealing with Halal Thoyyiban issues in functional food manufacturing and biotechnological industries.

The Halal philosophy focuses on risk minimization and is based on *Fiqh* (Islamic Jurisprudence). This philosophy can persuade the decision-making patterns with cognitive, affective and co-native (Wilson & Liu, 2011). In sustaining innovative bioactive marine base products, propagating Islamic values towards its marine animal care and the use of activities and scientifically related procedures, knowing the epistemological reasoning behind the "do and don'ts" of Islamic rules (*Fiqh halal-haram*) is indispensably essential [Mesyuarat Jawatankuasa Fatwa Negeri Selangor, 2012].

Conclusion

This write-up have tried to extrapolate critical issues and factors of pertinent to ongoing and future research innovations agenda in relation to bioactives products from marine based product exploitation. As such to ensure sustainable scientific based, novel Halal Thoyyiban products are commercial exploited and a have a success index perspective of Malaysian Halal Food Industry and marketing strategies.

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