



GLOBAL
HALAL SPHERE
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2019

Halal Sphere:
Where Diversity and Inclusivity Meet

Organised by:



Held on

21st - 22nd August, 2019

at the

INTERNATIONAL INSTITUTE OF ISLAMIC THOUGHT
AND CIVILISATION (ISTAC - IIUM),
INTERNATIONAL ISLAMIC UNIVERSITY MALAYSIA (IIUM)

Day 2 (Thursday, 22nd August 2019)

Parallel Sessions 4

09.00 – 10:00	Seminar Room 7 HOPPER VI	Seminar Room 8 HOPPER VII	Seminar Room 9 HOPPER VIII
	<p><i>Chairperson:</i> Dr. Nazariyah Yahaya</p> <p><i>Co-Chairperson:</i> Dr. Mohammad Aizat Jamaludin</p>	<p><i>Chairperson:</i> Dr. Syaza Azhari</p> <p><i>Co-Chairperson:</i> Dr. Nur Azira Tukiran</p>	<p><i>Chairperson:</i> Assoc. Prof. Dr. Rosnah Shamsudin</p> <p><i>Co-Chairperson:</i> Dr. Noor Faizul Hadry Nordin</p>
	<p>HOPPER 26: 'Aliya Afnan Mohd Nasir and Amalia Mohd Hashim - <i>Vortex assisted liquid-liquid extraction and purification of glycerin from cosmetic product</i> (ID:58)</p> <p>HOPPER 27: Hazwani Husain and Nur Huda Faujan - <i>Potential Application of Grey Oyster Mushroom Stem as Halal Meat Replacer in Imitation Chicken Nugget</i> (ID:36)</p> <p>HOPPER 28: Nur Syahiba Haseena Ahmad Sowhini, Muhammad Shirwan Abdullah Sani, Yumi Zuhani Has-Yun Hashim, Rashidi Othman, Mohd Hafidz Mahamad Maifiah and Mohd Nasir Mohd Desa - <i>Antibacterial Test, Toxicity and Application of Plant Seed Extracts: A Review</i> (ID:38)</p> <p>HOPPER 29: Amal Elgharbawy, Azrini Azmi and Hamzah Mohd Salleh - <i>Ionic Liquids: Promising Solvent for Halal Industry</i> (ID:12)</p>	<p>HOPPER 30: Nurfatim Syahirah Mohamed Ali, Atiqah Ruqayyah Zabidi, Mohd Nazmi Abd Manap, Shikh Mohd Shahrul Nizan Shikh Zahari and Nazariyah Yahaya - <i>Effect of Different Slaughtering Methods on metabolites of Broiler Chickens using Liquid Chromatography- Time of Flight- Mass Spectrometry (LC-TOF-MS)</i>(ID:22)</p> <p>HOPPER 31: Nurhusna Samsudin, Yumi Zuhani Has-Yun Hashim, Hamzah Mohd. Salleh - <i>In-silico approach in risk assessment of nutraceutical Properties</i> (ID:37)</p> <p>HOPPER 32: Nurulhidayah Ahmad Fadzillah, Nurul Widad Fitri Muhammad, Hamzah Mohd Salleh, Rashidi Othman and Abdul Rohman - <i>Physicochemical Properties of Dragon Fruit Peel Pectin and Commercial Pectin: A Comparison</i> (ID:24)</p> <p>HOPPER 33: Norhayati Hussain, Najjah Azhar and Nor Aqilah Abd Rahim - <i>Physicochemical qualities of chili padi Centil (Capsicum frutescens) powders at different drying temperatures</i> (ID:19)</p>	<p>HOPPER 34: Muhamad Nur Aminin, Kamarulzaman Nitty Hirawaty and Mohd Nawi Nollila - <i>Factors Influencing Agro-Food SMEs' Intention to Adopt Halal Traceability System</i> (ID:34)</p> <p>HOPPER 35: Rosnah Shamsudin, Hanny Zurina Hamzah, Kawamura Shuso, Eriko Yasunaga and Fauziah Mahat - <i>A Review : Nutrition Quality and Processing of Malaysia Strawberry</i> (ID:29)</p> <p>HOPPER 36: Zahir Uddin Mohammed Babar, Irwandi Jaswir, Mohd Hafidz, Wan Mohd Azizi, Solachuddin Juahari Arief and Qamar Uddin Ahmad - <i>Neuroprotective Potential of Water-Soluble Extract And Oil of Nigella Sativa (L.) Seeds Against Aluminium Chloride-Induced Neurotoxicity in Zebrafish Embryo Models</i> (ID:42)</p>
10:00 – 10:20	Tea Break Venue: Banquet Hall		
10:20 – 11:00	<p>Invited Speaker 2 Prof. Dr. Winai Dahlan, The Halal Science Center, Chulalongkorn University, Thailand Title: Practical Algorithms for Uplifting Halal Innovation and Research in New Paradigm of Halal for All Venue: Main Hall</p>		
11:00 – 11:40	<p>Invited Speaker 3 Prof. Dr Mohamed M. Mostafa, Gulf University for Science and Technology, Kuwait Title: Sentiment Analysis of Halal Food Venue: Main Hall</p>		
11:40 – 13.00	<p>Forum title: Halal sector in the era of industry 4.0: insight and implication</p> <p>Moderator: Prof Dr. Shuhaimi Mustafa, IPPH, Universiti Putra Malaysia Panellist 1: Prof. Dr. Marco Tieman, LBB International, Malaysia Panellist 2: Prof. Dr. Pakorn Priyakorn, Halal Standard Institute of Thailand (HSIT), Thailand Panellist 3: Mr. Romzi Sulaiman Halal Industry Development Corporation (HDC), Malaysia Venue: Main Hall</p>		
13.00	Photo-session		
13.20	Lunch & End of Day 2 Venue: Banquet Hall		

ABSTRACT OF PRESENTATIONS

- HOPPER 17: Mohd Hafidz Mahamad Maifiah, Makatar Wae-Hayee, Adilan Hniman and Nawawee Tohyeng - *Detection of Pork in Processed Meat Products by species-specific PCR for halal verification: Food fraud cases in Hat Yai, Thailand.* (ID: 54)
- HOPPER 18: Ismarti, K. Triyana, N. A. Fadzilah, H. M. Salleh and N. F. H Nordin - *Optimization of the Maillard reaction of bovine gelatin-xylose model using response surface methodology.* (ID: 16)
- HOPPER 19: Sarah Idris, Rosnah Shamsudin, Mohd Zuhair Mohd Nor, Mohd Noriznan Mokhtar and Siti Salwa Abdul Gani - *Physicochemical Composition of Different Parts of Cassava (Manihot esculenta Crantz) Plant.* (ID: 30)
- HOPPER 20: Widia Pangestika, Ahmad Al-Baarri, Anang Legowo, Anggun Puspitoasih, Mulyana Hadipernata and Wisnu Broto - *Hypoiodous Acid (HIO) potentially as Halal Preservative in Influencing towards Quality of Snake Fruit Cultivar Pondoh (Salacca edulis Reinw.) during Low Temperature Storage.* (ID: 57)
- HOPPER 21: Widayat Widayat, H Hadiyanto, D.A Putra, Izmi Nursafitri and Hantoro Satriadi - *Waste Cooking Oil Processing for Fatty Acid Methyl Ester and Mono Glycerides Production with Magnetite Catalyst.* (ID: 33)
- HOPPER 22: Nazariyah Yahaya, Atiqah Ruqayyah Zabidi, Farah Najiha Fauzi, Mohd Zuhairah Mohamed Jamil, Wan Kamillah Wan Ibrahim, Siti Salwa Abd. Gani and Zalina Zakaria - *Optimization of Polymerase Chain Reaction (PCR) method to Detect Porcine DNA in Cosmetic Cream.* (ID: 15)
- HOPPER 23: Ahmad Ni'Matullah Al-Baarri, Anang Mohamad Legowo and Fatma Puji Lestari - *Determination of Scavenging Activity and Physical Phenomenas Maillard Reaction Products from D-tagatose and Methionine.* (ID: 56)
- HOPPER 24: Stashia Eleaness Rosland Abel, Yus Aniza Yusof, Nyuk Ling Chin, Lee Sin Chang and Hasanah Mohd. Ghazali - *Physical Properties of Gum Arabic Powder at Various Particle Sizes.* (ID: 13)
- HOPPER 25: Nurfarhana Shaari, Rosnah Shamsudin, Mohd Zuhair Mohd Nor, Norhashila Hashim and Azman Hamzah - *Phenolic, Flavonoids and Anthocyanin Contents of Local Sweet Potato (Ipomoea batatas).* (ID:3)
- HOPPER 26: 'Aliya Afnan Mohd Nasir and Amalia Mohd Hashim - *Vortex assisted liquid-liquid extraction and purification of glycerin from cosmetic product.* (ID: 58)
- HOPPER 27: Hazwani Husain and Nur Huda Faujan - *Potential Application Of Grey Oyster Mushroom Stem As Halal Meat Replacer In Imitation Chicken Nugget.* (ID: 36)
- HOPPER 28: Nur Syahiba Haseena Ahmad Sowhini, Muhammad Shirwan Abdullah Sani, Yumi Zuhani Has-Yun Hashim, Rashidi Othman, Mohd Hafidz Mahamad Maifiah and Mohd Nasir Mohd Desa - *Antibacterial Test, Toxicity and Application of Plant Seed Extracts: A Review.* (ID: 38)
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- HOPPER 31: Nurhusna Samsudin, Yumi Zuhani Has-Yun Hashim, Hamzah Mohd. Salleh - *In-silico approach in risk assessment of nutraceutical properties.* (ID: 37)**
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HOPPER 31 (ID: 37)

In-silico Approach in Risk Assessment of Nutraceutical Properties

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Abstract

Dietary supplements, including those containing botanical ingredients and botanical-derived compounds, have been marketed to consumers globally for many decades. However, the legislative framework for such products remains inconsistent across jurisdictions internationally. A common problem, concerning these nutraceutical products, is deficient information and lack of data for assessing the hazards posed to human health. The main objective of this study is to explore the use of in silico tools in a risk assessment context of nutraceutical product, to relate properties of the molecular structure to the toxic effect of the chemical substance, by using principles and methods of computational chemistry. Further consideration of the actual impact of adverse events arising from nutraceutical food supplement usage will be helpful in guiding such issue as a potential for misidentification, and adulteration of botanical supplements by pharmacologically active substances.

Keywords: *In silico*, SAR, QSAR, risk assessment, nutraceutical

HOPPER 32 (ID: 24)

Physicochemical Properties of Dragon Fruit Peel Pectin and Commercial Pectin: A Comparison

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Abstract

Dragon fruit is a tropical fruit belongs to *Cactae* family of genus *Hylocereus*. Popularly known as 'buah Naga' in Malay, Dragon fruit is not only preferred for its unique taste, but this fruit is also nutritionally and medicinally attractive for consumers. The Dragon fruit flesh is usually eaten raw or it is blended into juice while the remaining peel is discarded. In order to minimize this waste from Dragon fruit consumption, an idea of transforming the peel of Dragon fruit into edible pectin has been proposed. Pectin can be found in food products as gelling agent and it is used to maintain the quality of foods. Market demand for pectin is increasing annually and in order to meet the supply-demand, researchers are working towards obtaining pectin from available non-conventional sources. In this study, pectin was extracted from Dragon fruit peel by hot acid extraction. Optimum conditions (pH 3.5, 75 minutes of extraction) were considered to yield the highest amount of pectin. Distilled water was used as solvent and the acidic environment was achieved with dilute HCl. The extracted pectin was categorized as high methoxyl pectin based on estimated degree of esterification (52%). FTIR analysis detected pectin's functional groups characteristics of carbohydrates, and the extracted pectin identity was confirmed by comparison with commercial pectin. Melting temperature (T_m) and melting enthalpy (ΔH_m) of the Dragon fruit peel pectin analysed by DSC were 122.01 oC and 385.40 mJ, respectively. The values were found to be higher than those of commercial pectin (107.11 oC and 77.81 mJ, respectively). Ash content, water and oil holding capacity (WHC, OHC) and swelling capacity (SC) are among other characteristics of extracted pectin that were analysed. Analysis of variance (ANOVA) of these characteristics showed there were no significant difference ($p > 0.05$) when compared with commercial pectin. However, there was a significant difference ($p < 0.05$) in moisture content between the Dragon fruit peel pectin samples and commercial pectin. Pectin gel was formulated from extracted pectin and tested for its cohesiveness, gumminess and hardness. Result obtained indicates the texture of this pectin gel has no significant difference compared with pectin gel made from commercial pectin. Therefore, we concluded that the Dragon fruit peel has a great potential to be an alternative pectin substitute.

Keywords: *Pectin extraction, dragon fruit peel, characterization, commercial pectin.*

In-silico approach in risk assessment of nutraceutical properties

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Abstract

Dietary supplements, including those containing botanical ingredients and botanical-derived compounds, have been marketed to consumers globally for many decades. However, the legislative framework for such products remains inconsistent across jurisdictions internationally. A common problem, concerning these nutraceutical product, is deficient information and lack of data for assessing the hazards posed to human health. The main objective is to explore the use of in silico tools in a risk assessment context of nutraceutical product, to relate properties of the molecular structure to the toxic effect of the chemical substance, by using principles and methods of computational chemistry. Further consideration of the actual impact of adverse events arising from nutraceutical food supplement usage will be helpful in guiding such issue as potential for misidentification, and adulteration of botanical supplements by pharmacologically active substances.

Keywords: In silico, SAR, QSAR, risk assessment, nutraceutical

1. Introduction

Nutraceutical can be define as a food or food product that reportedly provides a medical benefits, such as prevention and treatment of diseases. It is produced under GMP conditions and may range from isolated nutrients, dietary supplements and specific diets to genetically engineered foods, herbal products and process food (Mohammad et al., 2015). Example of nutraceutical products includes vitamins, mineral, herbal supplements, semi-purified substance from natural sources, plant extract, functional food and beverages, probiotics and topical application for skin care (Labadi, S. 2017). The therapeutics areas that is normally cover by nutraceuticals are anti-arthritis, cold and cough, prevention of certain cancer, diabetes, sleeping disorders, hypertension and osteoporosis (Pandey et al., 2010). Nutraceutical can be divided into three main segments which are natural products, dietary supplements and functional foods. Natural products and dietary supplements are segment with rapid growth due to high level of interest and demand by general public (Nutrition Business Journal, 2006). Such products are often comprehend as a more flattering as compared to pharmaceutical product as they are being seen as more natural and likely to incur minimum side effects (Teschke et al., 2013). Beside the availability of the nutraceutical products over the counter of supermarket, health food shop and pharmacies and lenient regulatory scrutiny before entering the market (Posadzki et al., 2013).

High cost incur by the modern disease treatment make consumer look for alternative or complementary beneficial product such as the appealing nutraceutical product. Only recently nutraceutical product been scientifically supported nutritional and medical evidence and become a potentially effective alternatives (Dillard and German, 2000). A sturdy regulation and assessment need to be develop and implement to give impact on consumer and to standardised the nutraceutical compound. Besides, requirement of the execution of clinical studies, provide basis for health claims, commercial positioning and functional claims of nutraceutical products should be evidence based that supported by convincing scientific data from well design studies. Moreover, nutraceutical products often taken as “self-medication” without concern from the medical doctor regarding any diseases that may lead to uncertainty in the observed effects. Therefore, there should be special aspects that need to be consider instead of basic design study that is similar to that of pharmaceutical studies. (Gao et al., 2014).

Considerably high number of cases that have been reported on the adverse effects of nutraceutical products that pose real risk to public (Rocha et al., 2016). The arising issue recently were the adulteration of nutraceutical products with pharmaceutical substance and accidental replacement of botanicals with some other toxic plant or substance (Stegelmeier et al., 2015). Besides, compounds such as alkenylbenzenes estragole and methyleugenol that are naturally contain in some botanicals are found to be genotoxic and hepatocarcinogenic based on animal study done by Scientific Committee on Food European Commission (SCF EC., 2001). Reports on human studies associated with the severity of effect of the consumption of botanicals range that caused elevation in blood pressure, acute liver failure requiring liver transplantation, tumors of the urinary tract and even death (Fujita et al., (2007); Nortier et al., (2009)).

Unravel the kinetic profiles and rectifying the bioavailability of nutraceutical properties and nutritional compounds posture some challenge especially in dealing with complex mixture derive from herbal plants. The main problem is to characterised the exact bioactive compound where regulating the bioactives intake is a challenge in term of variation in the plant composition. The variation further complicates the interpretation of different bioactives within botanical compound in nutraceutical that may exert either antagonistic or synergistic interaction(Schmitt and Farro, 2013).

Animal testing has been used to provide toxicological information, but in addition to the ethical consideration, it is both expensive and time consuming. Alternatives to animal data, i.e., non-testing data is therefore desirable and is highlighted to promote alternative methods for the assessment of hazards of substances. Non-testing data (or could be expressed as non-animal-testing data) includes, for example, in vitro data but can also be generated using in silico tools. In silico means within computer, and the term ‘in silico tools’ is collectively used to refer to methods as structure reactivity relationships (SARs), quantitative structure-activity relationships (QSARs) (Puzyn et al., 2010) and network pharmacology.

Animal studies for the type of toxicological information needed are both expensive and time consuming, and to that an ethical aspect is added. Alternative methods to animal testing are thereby requested. With the continuous maturation of computer technology, an increased use of in silico tools for non-testing data as structure-activity relationships (SARs), quantitative structure-activity relationships (QSARs), and pathway

and network analysis. This lead to the rapid elucidation of the complex relationships between compounds and their various activity target (Rubio-Perez et al., 2015). The main objective is to explore the use of in silico tools in a risk assessment context of nutraceutical products. In particular, try to relate properties of the molecular structure to the toxic effect of the chemical substance, by using principles and methods of computational chemistry.

2. Discussion

2.1 Risk assessment and regulation

The assessment criteria for the nutraceutical products are generally similar between some country such as Australia, USA and Europe (EU). Particularly, information related to requirement of basic information of the botanical substance and description of the botanical substance and description of manufacturing process (Low et al., 2017). However, jurisdiction regarding the specific toxicology data requirement, clinical trial data and adverse reaction report of nutraceutical product are mostly diversify. For example in term of requirement on specific toxicological studies, European Food Safety Authority (EFSA) is comparatively brief as compared to Therapeutic Goods Administration, Australia (TGA) and U.S. Food and Drug Administration (FDA) whose describe the necessary toxicity studies in more detail (Low et al., 2017). FDA even take an initiative to come out with a “Safety Testing Recommendation Matrix” that has been a good references for business operator as it recommend a different combination of toxicology data based on the historical used of the ingredients to determine the possible toxicity of their products. This matrix help the business operator in a way of reducing the cost and the hassle of conducting the toxicity study (FDA 2016).

Data on clinical trials are required by TGA guideline for risk assessment as TGA regulates the nutraceutical product as complementary medicine rather than food supplement (TGA 2016). EFSA on the other hand does not acquire such data and the fact that it is not obligatory either for FDA to provide the clinical trials data but they required at least to have a tolerability studies on adsorption, distribution, metabolism and excretion (ADME) studies to determine the safety margin for one products (FDA 2016).

The development of extraction technologies, pose a new risk related to botanical through the dynamic of economically motivated fraud. Moreover, there are some aspects that not been considered in the guidance documents for risk and safety assessment of nutraceutical products. Despite the uncertainty of the authentication and differences in regulation, the global nutraceutical market has been valued at USD 109.8 billion and expected to grows to an expected value of USD 180 billion by 2020 (Persistence Market Research 2015). Therefore, the current issues should set the direction in the nutraceutical field that highlight the evidence-based nutraceutical approach can make important contribution to public health.

2.2 SAR and QSAR

SAR analysis is the identification of chemical properties or specific fragments of the molecular structure involved in an observed or measured effect. A QSAR model approximates the relationship between the molecular structure and a biological activity in a quantitative

manner (Eriksson, et al., 2003). The QSAR model can be used to determine SAR. Prior to a quantitative correlation, the biological or toxic activity as well as the chemical and structural properties are defined with numerical values. The outcome of biochemical and toxic effects of particular substances were measured in in vitro assays. QSAR modelling begins with a set of chemical structures that are assumed to act by the same mechanism of action, and then follows a stepwise process as the general pathway illustrated in Figure 1.

In order to enhance the regulatory acceptability and use of QSAR, the organisation for economic co-operation and development (OECD) outlined principles for QSAR validation (OECD, 2007). According to these principles, a QSAR model should be associated with 1) a defined endpoint, 2) an unambiguous algorithm, 3) a defined domain of applicability, 4) appropriate measures of goodness-of-fit, robustness and predictivity, and if possible, 5) a mechanistic interpretation. The aim of this principle is to ensure that selection of the chemical descriptors is well considered in relation to the endpoint of the investigation, and that any association found between the chemical descriptors and the endpoint is documented (OECD, 2007).

2.3 Pathway and network analysis

In recent years, with an increasingly in-depth understanding of the structure and function of compounds, a series of new technologies and methods have been applied to the development of medicinal plants (Yi et al., 2016). If we can establish a quick and convenient pathway by which to first accurately predict a large number of chemical compounds and then, based on these results, perform in vivo and in vitro pharmacological experiments for verification, this procedure will significantly improve the efficiency of evaluating the chemical activities of nutraceutical product.

The continuous maturation of computer technology, the in silico approach of utilizing a computer platform to calculate the combinations of simulated compounds and targets has become increasingly accurate. In addition, the development of network pharmacology technologies has enabled the rapid elucidation of the complex relationships between compounds and their various activity targets (Rubio-Perez et al., 2015).

Its complexity is not only reflected in the composition of the chemical constituents but also embodied in the network of relationships between the prescription and the human body and the exertion of pharmacological effects through multiple channels, multiple targets and the overall regulatory mechanism (Zhang et al., 2016).

Considering the medicinal plant as the object and virtual computational screening as the central methodology within nutraceutical informatics, and using network pharmacology as the technical means, we have employed a set of effective and accurate methods to reveal the pharmacological basis of the effects of medicinal plant materials and predict the potential bioactivity of their compounds. The approach proceeds from the selection of the plant active compounds to virtual screening and evaluation of the targets, related signalling pathways and disease networks (Yi et al., 2018). Techniques from virtual computational screening and network pharmacology are used to construct a complete technical routine for this methodology. The first step is to confirm the research significance of the plants. These medicinal plants can be organized into three categories: (1) common herbs with a more complex mechanism than

that of other herbs; (2) herbs with a long history of traditional usage but fewer studies on their phytochemistry and haemacology; and (3) herbs with a history of traditional usage but now with a new utilization (Yi et al., 2018).

The second step is the organization and collection of the natural products to construct the natural products database. The third step is the pre-treatment of these compounds, including drug-like analysis, ADME/T (absorption, distribution, metabolism, excretion and toxicity) prediction and the exclusion of false-positive compounds. The fourth step is the core technique of this methodology, the *in silico* virtual screening. This step were design by combining three different theoretical bases: the first is virtual target fishing based on pharmacophore theory; the second is dual validation based on small molecule shape similarity theory; and the third is compound-target analysis based on docking. The fifth step is the analysis of the set of targets identified. By utilizing the technical methods of network pharmacology and different protein information databases and websites, we can analyse the relationships of signalling pathways, pathological pathways and related diseases with potential targets. Finally, the network of relationships was constructed among medicinal plants, natural compounds, biological targets, signalling pathways, and diseases. We thereby elucidate the mechanistic basis of the effects of the natural compounds in medicinal plants and predict their potential pharmacological activities (Yi et al., 2018).

3. Conclusion

The alternative strategies for the assessment of hazards to complement *in vitro* and *in vivo* studies for nutraceutical products has been explore. The potential of using different *in silico* methods for this purpose has been investigated and QSAR models have been studied. Information contained in two diverse datasets of nutraceutical product was searched with SAR and QSAR methods. Wide-ranging complete technical route that utilizes a series of *in silico* approaches to reveal the pharmacological basis of the effects of medicinal plants were proposed. This *in silico* methodology can resolve the status of medicinal plants that are difficult to study on a practical level and can predict and clarify the mechanisms of the active ingredients in nutraceutical product. Through more practical researches and development examples to upgrade the entire process of *in silico* methodology, we believe that in the future, this methodological process will enable the discovery of new active compound more efficiently, accurately and quickly. This methodology will be more widely usable in future work on revealing and predicting the basis of nutraceutical materials.

Conflict of Interest

No conflict of interest

References

- Dillard, C. J., and German, J. B. (2000). Phytochemicals: nutraceuticals and human health. *J Sci Food Agric*, 80, 1744–1756.
- Eriksson, L., Jaworska, J., Worth, A.P., Cronin, M.T.D., McDowell, R.M., Gramatica, P. (2003). Methods for reliability and uncertainty assessment and for applicability evaluations of classification and regression-based QSARs. *Environmental Health Perspectives*, 111, 1361-1375.
- Food and Drug Administration (FDA) (2008). Guidance for Industry: genotoxic and carcinogenic impurities in drug substances and products: recommended approaches (Draft guidance). Available from: <http://www.fda.gov/ohrms/dockets/98fr/fda-2008-d-0629-gdl.pdf>. Accessed 1 July 2019.
- Fujita, Y., Terui, K., Fujita, M., Kakizaki, A., Sato, N., Oikawa, K. et al., (2007). Five cases of aconite poisoning: Toxicokinetics of aconitines. *J Anal Toxicol*, 31, 132–137.
- Gao, B., et al. (2014). Platelet P2Y₁₂ receptors are involved in the haemostatic effect of notoginsenoside Ft₁, a saponin isolated from *Panax notoginseng*. *Br. J. Pharmacol*, 171(1), 214.
- Labadi, S. (2017). Pursuing health through nutraceuticals but halal consumer beware. Retrieved on June 12, 2019 from Website: www.salamgateway.com/en/home.
- Low, T. Y., Wong, K. O., Yap, A. L. L., De Haan, L. H. J. And Rietjens, I. M. C. M. (2017). The regulatory framework across international jurisdictions for risk associated with consumption of botanical food supplements. *Comp. Rev. Food Sci. Food Saf.*, 16, 821-834.
- Mohammad, A. A., Baharuddin, A. S. and Ruskam, A. (2015). Halal industry in Singapore: A case study of nutraceutical products. *Sains humanika*, 4(2), 35-40.
- Nortier, J. L., Martinez, M-C. M., Schmeiser, H. H., Arlt, V. M., Bieler, C. A., Petein, M. et al., (2009). Urothelial carcinoma associated with the use of a Chinese herb (*Aristolochia fangchi*). *N Engl J Med* 342, 1686–1692.
- Nutrition Business Journal, 1:2, September 1996.
- OECD, 2007. Organisation for Economic Co-operation and Development. Guidance document on the validation of (quantitative) structure-activity relationships [(Q)SAR] models. ENV/JM/MONO(2007)2 OECD.
- Pandey, M. Verma, R. K., and Saraf, S. A. (2010). Nutraceuticals: new era medicine and health. *Asian J Pharma Clin Res*, 3, 11-15.
- Persistence Market Research. (2015). Dietary supplements market - Global study on dietary supplements: Botanical supplements to be the largest market by 2020. Available from: <http://www.persistencemarketresearch.com/market-research/dietary-supplements-market.asp>. Retrieved at 18 July 2019.
- Posadzki, P., Watson, L., Ernst, E. (2013). Herb–drug interactions: an overview of systematic reviews. *Br J Clin Pharmacol*, 75, 603–618.

Puzyn, T., Leszczynski, J., Cronin, M.T.D. (Eds.), 2010. Recent advances in QSAR studies - Methods and applications. Springer.

Rocha, T., Amaral, J. M. S., and Oliveira, M. B. P. P. (2016). Adulteration of dietary supplements by the illegal addition of synthetic drugs: a review. *Compr Rev Food Sci Food Saf*, 15, 43–62. <https://doi.org/10.1111/1541-4337.12173>.

Rubio-Perez, C., et al. (2015). In silico prescription of anticancer drugs to cohorts of 28 tumor types reveals targeting opportunities. *Cancer Cell*, 27(3), 382–396.

SCF EC. (2001). Opinion of the Scientific Committee on Food on methyleugenol (4-Allyl-1,2-dimethoxybenzene). Available from: https://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scf_out102_en.pdf. Accessed 29 May 2019.

Schmitt, J., and Ferro, A. (2013). Nutraceuticals: is there goods science behind the hype?. *Br J clin Pharmacol*, 75(3), 585-587.

Stegelmeier, B. L., Brown, A.W., and Welch, K. D. (2015). Safety concerns of herbal products and traditional Chinese herbal medicines: dehydropyrrolizidine alkaloids and aristolochic acid. *J Appl Toxicol*, 35, 1433–1437. <https://doi.org/10.1002/jat.3192>.

Teschke, R., Frenzel, C., Glass, X., Schulze, J., and Eickhoff, A. (2013). Herbal hepatotoxicity: a critical review. *Br J Clin Pharmacol*, 75, 630–636.

Therapeutic Goods Administration (TGA). 2016a. Australian regulatory guidelines for complementary medicines (ARGCM) V6.0. Available from: <https://www.tga.gov.au/publication/australian-regulatory-guidelinescomplementary-medicines-argcm>. Accessed 10 July 2019.

Yi F, et al. (2016). In silico approach for anti-thrombosis drug discovery: P2Y1R structure-based TCMs screening. *Front Pharmacol.*, 7, 531.

Yi F, et al. (2018). In silico approach in reveal traditional medicine plants pharmacological material basis. *Front Pharmacol.*, 7, 531.

Zhang Y, et al. (2016). Pathway of PPAR-gamma coactivators in thermogenesis: a pivotal traditional Chinese medicine-associated target for individualized treatment of rheumatoid arthritis. *Oncotarget*, 7(13), 15885–15900.

Tables and Figures

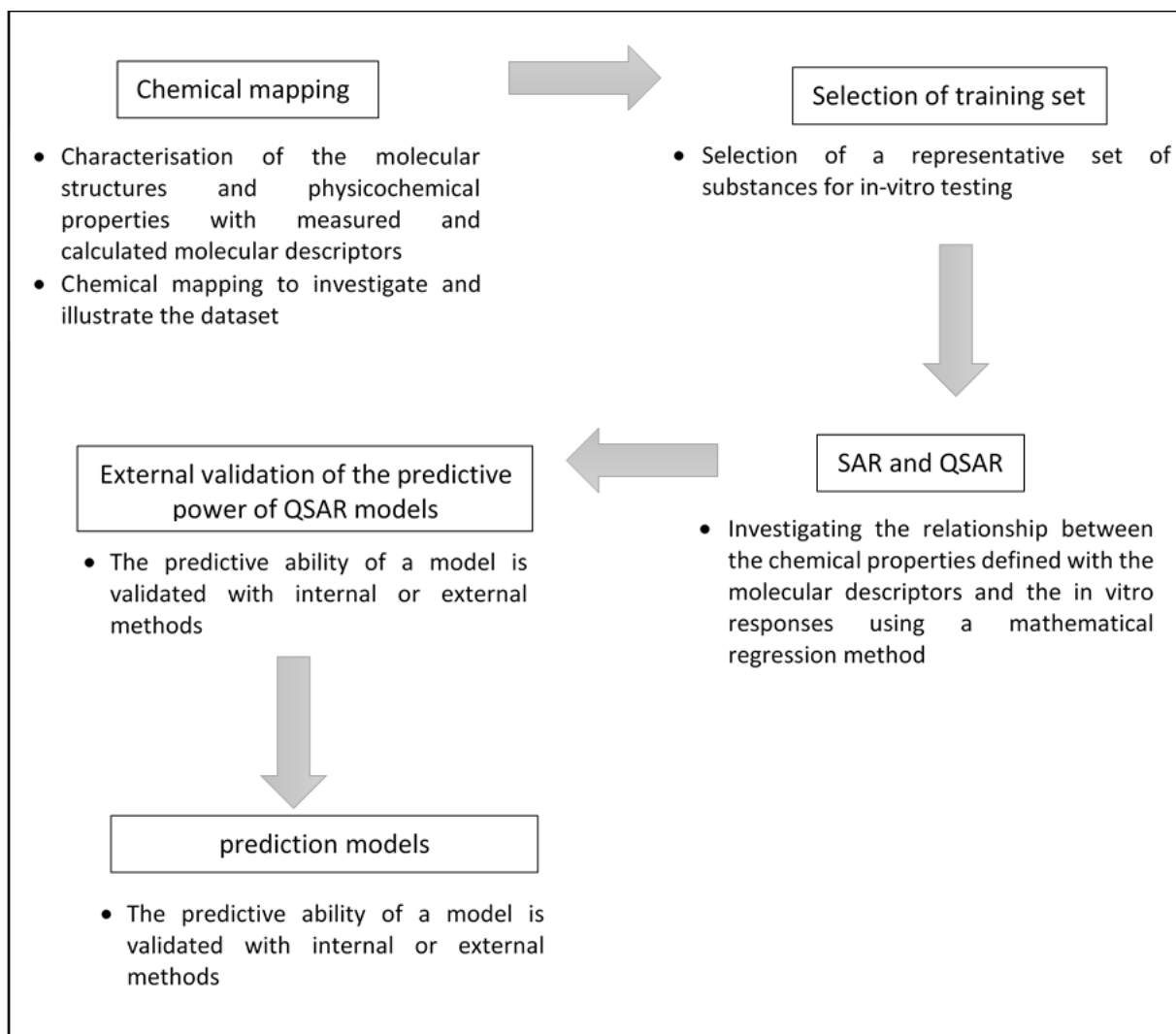


Figure 1. Stepwise QSAR/ in silico approach