



i-CAST

# IIUM-iCAST 2010

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*26-29 November 2010  
Vistana Hotel, Kuantan*

*"The Science of  
Traditional Practices  
in Health and Disease"*





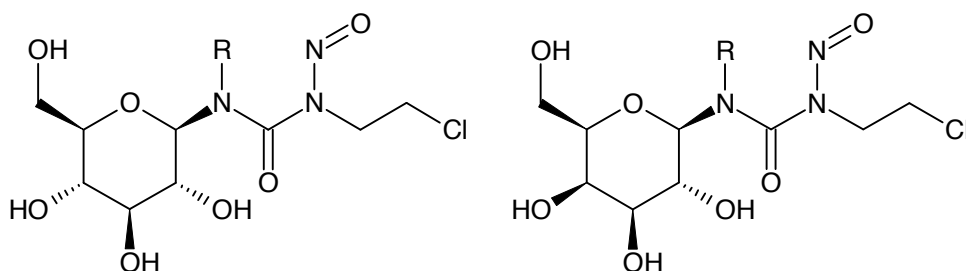
ID 071      28 Nov/21 Dhul al-Hijjah      Sunday      1155-1215      Ballroom

### Quantum Chemical Quantitative Structure Activity Studies of Anticancer Activity of Aldohehexose chloroethylnitrosourea Analogs

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Quantitative structure activity relationship involving 18 aldohexose chloroethylnitrosourea compounds having anticancer activity against Ip-Implanted Murine L1210 Lymphoid Leukemia, is investigated using semi-empirical quantum chemical AM1 methods.



Quantum chemical methods are used to calculate several electronic and molecular properties of these compounds and these properties are used to obtain the best QSAR using statistical procedures. A best QSAR with correlation coefficient of  $R^2 = 0.7270$  is established with four theoretical molecular descriptors. The QSAR obtained in our study can be used to predict the anticancer activity of new aldohexose chloroethylnitrosourea analogs, without resorting to any experimental studies.

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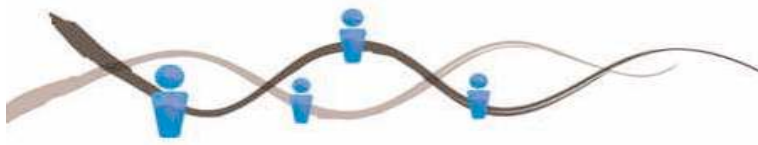
### Bioactivities of $\alpha$ -mangostin from *Garcinia malaccensis* Hk.f

Farah Syahidah A. ZOHRI, Muhammad TAHER, Deny SUSANTI, Sauba NAKAZIBWE, Solachuddin JA ICHWAN

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Guttiferae family is well-known to have a wide range of phytochemical constituents and bioactivities. A phytochemical investigation of *Garcinia malaccensis* lead isolation of  $\alpha$ -mangostin,  $\beta$ -mangostin and a triterpenoid.  $\alpha$ -Mangostin, a xanthone has a lot of health benefits. Many studies have been reported to investigate the biological activities of  $\alpha$ -mangostin. The present study was carried out to evaluate the antimicrobial, antioxidant and anticancer activities of  $\alpha$ -mangostin. Its structural determination was done based on its spectroscopic analysis.  $\alpha$ -Mangostin was tested for antimicrobial sensitivity via disc diffusion method against 4 bacteria. Results showed that *S. aureus* culture formed a clear inhibition zone. The diameter of zone of inhibition observed was 8 mm and minimum inhibition concentration (MIC) value was 0.025 mg/mL and minimum bactericidal concentration (MBC) value was 0.1 mg/mL, indicated that  $\alpha$ -mangostin is a bacteriostatic and bactericidal agent which correlates to presence of hydroxyl group in its structure. In antioxidant properties tests, dot-blot DPPH staining showed a positive antioxidant activity of  $\alpha$ -mangostin. In FTC method,  $\alpha$ -mangostin was proved to be a good lipid peroxidation inhibitor, whereas in DPPH free radical scavenging activity method, it has very weak scavenging effects on free radicals. In antiproliferative assay,  $\alpha$ -mangostin exhibited activity against K562 and showed different activity against HSC3 and H1299 cell lines. Against K562, it exerted the value of IC<sub>50</sub> 20  $\mu$ g/mL. This study can form a foundation for future studies in investigating of biological activities of  $\alpha$ -mangostin and developing the natural abundant in improving a healthy community.





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**Amino and fatty acid compositions in haruan traditional extract**Che Ku DAHLAN-DAUD<sup>1</sup>, Abdul M MAT JAIS<sup>1</sup>, Zuraini AHMAD<sup>1</sup>, Abdah MD AKIM<sup>1</sup>, Aishah ADAM<sup>2</sup><sup>1</sup>. Dept. Biomed Sci, Faculty Med and Health Sci, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor; <sup>2</sup>Dept Pharmaceutical Sci, Faculty of Pharmacy, UiTM, 40450 Shah Alam, Selangor

Evaluation of amino and fatty acids compositions in Haruan Traditional Extracts (HTE) was done using HPLC and GC methods. The HTE contained at least 17 amino acids with glutamic acid, glycine, leusine, aspartic acid, proline, alanine and arginine are the most, with values 1.87 - 43.1293 mg/g, 21.80 - 80.85 mg/g, 7.85 - 40.19 mg/g, 13.85 - 44.07 mg/g, 9.4861 - 45.46 mg/g, 11.38 - 35.25 mg/g and 5.99 - 21.79 mg/g, respectively. Meanwhile, the highest percentage of fatty acids is palmitic acid; 3.54 - 26.84 % of total protein. The others major fatty acids are stearic acid, oleic acid and linoleic acid with values 3.25 - 15.90 %, 1.40 - 27.68 %, 0.51 - 7.82 % of total protein, respectively. HTE also found to have 4 extra bioactive compounds labelled as 1 to 4 on chromatographic tracing which in line with previously finding. It is concluded that the HTE is containing all the important amino acids plus some fatty acids, which is the basis to conduct antioxidant composition in both fresh Haruan and the HTE which was claimed to have wound healing properties. Comparative study was also carried out in various other extraction protocols, including commercial product.

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**Study of antihyperglycaemic properties of selected Malaysian antidiabetic plants in cultured 3T3-L1 cells**Nuraniza AZAHARI, Muhammad M A K KHATTAK, Muhammad TAHER, Solachuddin JA ICHWAN  
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Diabetes Mellitus is a metabolic disease occurring worldwide caused by defects in insulin secretion, insulin action, or most commonly both. Diabetes mellitus is probably the fastest growing metabolic disease in the world and as knowledge of the heterogeneous nature of the disease increases so does the need for more challenging and appropriate therapies. The aim of the research is to evaluate the antidiabetic properties of selected antidiabetic plants used in the treatment of diabetes mellitus. The selection of plants was based on traditional reputation of usefulness in treating diabetes. Water extracts of *Syzygium Polyanthum*, *Peronema Canescens*, *Orthosiphon Stamineus*, *Lagerstroemia Speciosa*, *Momordica Charantia*, *Tinospora Crispa*, *Archidendrau Jiringa*, *Cinnamomum Zeylanicum*, and *Andrographis Paniculata* were selected. Insulin was used as a positive control. The plants were studied on the bioactive peptides (adipokines) using an in-vitro model. 3T3-L1 adipocyte cell line is selected for this study because it plays an important role in lipid storage and glucose homeostasis. The first test is to know the ability of the plants to induce preadipocyte to adipocyte cell by using the mixture of dexamethasone, 1-isobutyl-3-methylxantine and the plant extracts. Then, continue with the MTT assay to study the toxicity level in order to get appropriate dose of the extracts. After that, protein analysis is conducted to demonstrate the plant activity that mimics insulin action. Adipogenesis, adipolysis, adiponectin and leptin protein were analyzed to assess the effect of the extract on lipid synthesis and degradation in the cultured 3T3-L1 cells by using ELISA kit. The result confirms that a preadipocyte cell was differentiated to adipocyte. Preliminary result shows that *A. Paniculata* and *L. Speciosa* extracts have strong activity in inducing lipid formation.



### **ID 152: Growth suppression of non-small lung carcinoma cell H1299 transfected with p53 and p73 $\beta$**

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p53 gene has been hailed to have important roles in maintaining genomic integrity. The critical roles of this tumor suppressor in cell cycle, DNA repair, and apoptosis profoundly contribute to development of cancer. p53 mutations have been found in almost fifty percent of all cancer types, including lung cancers. Hence, the idea of restoring the normal function of p53 gene by exogenous p53 replacement therapy has been discussed and investigated in order to overcome cancer. However, introduction of wild-type p53 protein is unable to induce apoptosis in all tumor cases, at least in part, due to their resistance to exogenous p53.

p73 $\beta$  has been regarded as one of the strongest candidate as it is similar to p53 in many aspects: structural homology, transactivation of p53-downstream genes, and induction of apoptosis. It has been reported that a similar therapeutic strategy can be successfully applied in p73 activation as well. Interestingly, the mutation of this gene has been rarely found in cancer, suggesting different mechanism or regulation pathway of this gene. The aim of this study is to compare the tumor suppressor activity of p53 and p73 $\beta$ , on p53  $-/-$  non-small cell carcinoma cells H1299 was conducted. Stable and transient transfection of p53 and p73 $\beta$  constructed in pCMV plasmid was conducted through chemical mediated transfection. Introduction of exogenous expression of p53 significantly suppress colony formation of H1299 cells under G418 selection while p73 $\beta$  could partially suppress the colony formation. Consistently, exogenous p53 and p73 $\beta$  raise expression of p21/Waf gene. These results show overlapping regulation performed by p73 $\beta$  which suggest its application as alternative candidate in gene therapy.

### **ID 154: Production of recombinant p53 protein by PCR based site –directed mutagenesis of plasmid DNA**

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Cancer is a major burden of disease worldwide. Each year, tens of millions of people are diagnosed with cancer around the world, and more than half of the patients eventually die from it. It is a multifaceted disease, but a common feature of most tumors is that they harbor single or more genetic mutations that allow them to proliferate outside their normal growth restraints. Up to now, conventional treatments such as surgery, chemotherapy, and radiation, are commonly used for the treatment of all cancers. Despite these advancements, cancer morbidity and mortality is unacceptably high since some of these treatment approaches are highly invasive and sometimes have only a palliative effect. For this reason, gene therapy has been developed and considered as a new approach that may effective in combating cancers. In this study, we conduct a research aiming to p53, a gene that harbor most mutation in cancer. A construct of human recombinant protein that mimics specific hot-spots mutation of p53 gene in codon 248 was generated through Polymerase Chain Reaction (PCR) site-directed mutagenesis. This generated recombinant protein, (pCMV-p53R248Q) was transfected to p53-null-H1299 cells, together with wild-type p53 (pCMV-p53) and blank vector (pCMV) as control. For 3 to 4 weeks, the cell was cultured in the presence of G418 and stained with Giemsa for colony formation assay. The result has shown that, the cells that were transfected with pCMV-p53 suppressed the colony growth. However, the genetically engineered pCMV-p53R248Q shows neither suppressed nor effects on cells proliferation. The expression of p21 gene, the major transcriptional target of p53 that regulates cell cycle progression at G1 was also confirmed via real time polymerase chain reaction (qPCR). This result could determine the possibilities and development of other recombinant protein using site directed mutagenesis can be used to treat or prevent cancer as part of gene therapy in the future.