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Mechanisms of Anti-proliferative Effect of *Garcinia hombroniana* Essential Oils Leaves in MCF-7 and MCF-7/TAMR-1 Human Breast Cancer Cell Lines

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Breast cancer is the most common cancer affected women and the incidence rate is increasing yearly throughout the world. Tamoxifen is the first-line chemotherapeutic drug used in treating breast cancer patients. However, gynaecological complications and drug resistance are among the major drawback effects of tamoxifen. *Garcinia hombroniana* (GH) (seashore mangos teen) is a plant that has been reported to possess good cytotoxic effect against the growth of various human cancer cell lines, including the MCF-7. For this reason, the aim of this study was to further investigate the anti-proliferative and apoptotic effects of the essential oil extracted from the leaves of GH against two different types of breast cancer cell lines, MCF-7 and MCF-7/TAMR-1. The essential oil was extracted by hydrodistillation process from the leaves of GH. The anti-proliferative effects of the essential oil against MCF-7 and MCF-7/TAMR-1 cancer cell lines were determined using MTT assay and measured by a microplate reader. The mechanism of cell death was determined using Annexin V-FITC/propidium iodide staining assay and quantitatively measured by flow cytometry. The human non-cancerous breast cell line, MCF-10A was also included in both assays as comparative control cells to the MCF-7 and MCF-7/TAMR-1 cells. The results showed that the GH essential oil exhibited anti-proliferative effect against the growth of both MCF-7 and MCF-7/TAMR-1 cells following dose- and time-dependent manners, with an IC50 of 35.22 µg/mL and 17.67 µg/mL, respectively. Importantly, it exhibited low toxicity effect against the non-cancerous human breast cell line, MCF-10A, with an IC50 of 76.11 µg/mL. Additionally, flow cytometric analysis also further confirmed that the cell death induced by GH essential oil occurred via the mechanism of apoptosis. This study concluded that the essential oil of GH exhibited potent anti-proliferative effects against both MCF-7 and MCF-7/TAMR-1 human breast cancer cells. Based on the IC50 values, the MCF-7/TAMR-1 was more sensitive towards the GH essential oil treatment. Importantly, GH essential oil demonstrated low cytotoxicity towards the non-cancerous breast cell line, MCF-10A. These findings may at least in part explain to the selectivity of GH essential oil in killing breast cancer cell lines but not in normal counterpart. Besides its selective cytotoxic effect, the growth inhibitory action of GH essential oil against MCF-7 and MCF-7/TAMR-1 human breast cancer cells also mediated by apoptosis. Therefore, GH essential oil could be developed as a new, selective and potent anticancer agent in future.

Keywords: *Garcinia hombroniana*, Breast cancer, Tamoxifen resistant, Apoptosis, Cytotoxicity.

Analysis of OTUB1 Expression in Human Breast Adenocarcinoma Cell Line MCF7 and Human Breast Epithelial Cell Line MCF10A

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The process of ubiquitination is highly dynamic and reversible by the action of specialized enzymes known as deubiquitinases (DUBs). DUBs have essential roles in the ubiquitin system through their abilities to specifically remove ubiquitin from target proteins. A growing body of literatures have identified that OTUB1, one of the members of the ovarian tumour proteases (OTU) family of DUBs has a critical role in cancer initiation and progression. This study is to compare the expression of OTUB1 in human breast adenocarcinoma cell line MCF7 and human epithelial cell line MCF10A. Expression of OTUB1 in MCF7 and MCF10A was analysed by quantitative real-time PCR. Relative quantification of result was using $^{\Delta\Delta}$Ct method. Mann-Whitney test was used to detect the difference between the expression. Our study shows that the higher expression of OTUB1 in breast cancer cells MCF7 compared to normal epithelial breast cell MCF10A using qPCR is not significant. These finding is supported by bioinformatics analysis, in which 80% of the OTUB1 probes from selected microarray datasets confirmed that OTUB1 expression is higher in MCF7. Therefore, further gene knockdown study should be done in future in order to uncover the complex roles and functions of OTUB1 in cancer-associated pathways.

Keywords: Gene Expression, OTUB1, MCF7, MCF10A

Levels of Perfluorooctane Sulfonate (PFOS) and Perfluorooctanoic Acid (PFOA) in Home and Commercially Produced Poultry Eggs in Malaysia

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Perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) are the two major perfluorinated compounds (PFCs), widely used in products pertaining to their water and grease repellent properties. Their persistence nature and potential toxicity had raised substantial concern towards health effects. In human, food consumption was reportedly to be a significant source of exposure for both PFOS and PFOA. Hence, the objectives of this study were (1) To determine the level of PFOS and PFOA in the yolk of poultry eggs in Malaysia; (2) To develop and validate an analytical method for PFOS and PFOA using LC-MS/MS; (3) To compare the level of PFOS and PFOA between home and commercially produced chicken eggs; (4) To compare the level of PFOS and PFOA in chicken, duck and quail eggs. A total of 47 poultry egg yolk samples were extracted by simple protein precipitation technique using acetonitrile. The analytical method was developed using LC-MS/MS and validated based on FDA's Bioanalytical Method Validation guideline. The result revealed that PFOS was quantitatively detected in six samples with the concentration range between 0.5 to 1.01 ng g^{-1}. Among these, five samples were from home produced chicken eggs, and one sample was from a quail egg. The level of PFOA in all samples were below the quantifiable limit (<0.1 ng g^{-1}). This indicated that the contamination of PFCs in poultry eggs are mostly attributed to the nature of free foraging animals which have direct contact with the contaminants in soils and feeds. In conclusion, a fast and robust analytical method for analyzing PFOS and PFOA in egg yolk samples using LC-MS/MS was successfully developed and validated. The presence of these emerging contaminants in this study, signified the widespread pollution in the environment. Further study on risk assessment towards dietary exposure of PFCs are suggested.

Keywords: Perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA), poultry eggs, liquid chromatography tandem mass spectrometry (LC-MS/MS)

PEGylated Gold Nanoparticle (PEG AuNP) Development for Enhancement of Red Cell Antibody Agglutination Reaction

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Enhancing potentiators such as Low Ionic Strength Solution (LISS) and Polyethylene Glycol (PEG) have been widely used to fasten the red blood cell (RBC) antibody agglutination reaction. Gold nanoparticles with its inert and tunable property, have been proven in facilitating this reaction. Hence, this study aimed to develop an alternative enhancing potentiator for RBC antibody agglutination by using the combination of PEG and gold nanoparticle (PEG AuNP). One step synthesis via conjugation has been used for the development of PEG AuNP in the presence of sodium hydroxide (NaOH) resulted in the fast formation of PEG-coated gold nanoparticle. Characterisation of the newly developed solution was performed using UV-VIS spectrophotometer at room temperature across the spectral wavelength of 200 nm until 700 nm. Antibody screening test for three samples were performed comparing between enhancing potentiators (LISS, PEG, Gold, and PEG AuNP), and between different PEG AuNP concentrations at antiglobulin phase for RBC antibody agglutination reaction. PEG AuNP was successfully synthesised resulted from colour changes from transparent to violet and showed the maximum absorbance at 565 nm. The PEG AuNP solution showed similar reaction score as compared to LISS and PEG alone in antibody screening test. There was no significant difference in agglutination score between various concentration of PEG AuNP (p = 0.4). The newly developed PEG AuNP is capable to potentiate RBC antibody agglutination and thus can be a substitute solution for this purpose.

Keywords: PEG, gold nanoparticle, RBC agglutination reaction, antibody screening

Development and Validation of Questionnaire to Assess Knowledge, Attitude and Perception Among Nurses on Blood Transfusion Management: Nursing Responsibility and Patient Management

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In clinical practice, transfusion of blood products was often used to improve the clinical condition of patients. However, error in blood transfusion practice jeopardizing safe transfusion and may lead to life-threatening consequences to the patients. Hemovigilance program over the year continue to report, human error remains the greatest risks in safe blood transfusion. In Malaysia, reported transfusion reaction due to incorrect blood component transfusion was 0.73%, and the majority (80%) occur in the clinical ward. Nurses play a central role in ensuring safe blood transfusions, as more than half of the steps in blood transfusion are dependent on the nurse's awareness and skills. Sufficient knowledge, good attitudes and perception among nurses were essential to ensure safe practice in patient management. However, there was no validated questionnaire available to assess nurses' knowledge, attitude and perception in patient management related to blood transfusion. To develop and validate a questionnaire about the knowledge, attitude and perception among nurses on blood transfusion management**.** A cross-sectional study was conducted among nurses at the Clinical Complex (CC) of Advanced Medical and Dental Institute (AMDI), Hospital Kepala Batas and Hospital Seberang Jaya, Penang, Malaysia. The study used a self-administrated questionnaire. The validation involved content validation, construct validity, internal consistency and test-retest for reliability. A total of 210 nurses were responded. The Kaiser-Meyer-Olkin measure of sampling adequacy (KMO) was 0.60 and Bartlett's test of Sphericity was significant (P<.001). The internal consistency for knowledge was 0.549, attitude was 0.713 and perception was 0.586. The questionnaire on nurse' attitude was valid and reliable with good items that enables it used for accessing nurse's attitude in blood transfusion patient management. While, items on nurse's knowledge and perception need to be review and once this is complete, confirmation of the stability of the domains will be included in the next stage.

Keywords: Questionnaires development and validation, Blood transfusion management, Nurses KAP

Pharmacodynamic Effects Between Herbs and Chemotherapeutic Drugs: A Systematic Review

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Besides standard chemotherapeutic drugs, the use of herbal remedies has been steadily increased as one kind of complementary and alternative medicine among cancer patients. Herb-drug interactions (HDI) may exist and a number of evidence-based studies have been conducted over the past decades. This review aimed to systematically compile and analyze current studies related to the HDI and pharmacodynamic (PD) effects between herbs and chemotherapeutic drugs from year 2008 to 2019. All related articles were searched- via electronic databases and selected based on the predefined keywords and inclusion criterias. The data of the studies were extracted according to the bioactive constituents, anticancer drug, type of cancer, study design, mode of action and modulatory effect on PD after the HDI. A total of 63 related articles were included, most of the studies demonstrated synergism therapeutic effect (67%), followed by attenuation drug-induced side effect by herb (11%), adverse therapeutic effect (9%), antagonism (7%) and no change of therapeutic effect (6%). *In vitro* studies were the highest experimental design conducted for the determining the pharmacodynamic effects between herbs and chemotherapeutic drugs. Only 3 case reports, 1 cohort studies and 1 clinical studies were found to be related to adverse effect modulation. More than 20 modes of action involved in HDI-modulated PD effects. Apoptosis was reported to be the major mode of action (12%), followed by caspase activation (9%) and reactive oxygen species generation (9%). In conclusion, all included articles were systematically reviewed based on the limited numbers of reported *in vitro* findings. Therefore, this suggests that more studies focusing on HDI and PD effects between herbs and chemotherapeutic drugs are necessary to thoroughly investigate their effects and safety, especially for the benefits of cancer patients.

Keywords: pharmacodynamic, herb, chemotherapeutic drugs, systematic review

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Apoptosis Signalling Pathways of Zerumbone Isolated from *Zingiber Zerumbet* – A Systematic Review

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Zerumbone extracted from *Zingiber zerumbet* is well known to have anti-cancer properties. The aim of this systematic review is to evaluate the anti-cancer effect of Zerumbone via its apoptosis pathways. Relevant articles were selected based on the specific inclusion criteria. Articles chosen for this systematic review were between January 2008 to December 2018. Relevant articles were identified through an extensive search in ScienceDirect, PubMed, Google Scholar and Scopus. The literature searches of the electronic databases combined the following key words: anticancer, apoptosis, Zerumbone and *Zingiber zerumbet*. *In vitro* studies were shown to be the most used study design. Evidently, the antiproliferative activities of Zerumbone were shown to induced by its apoptosis signalling pathway.

Keywords: anticancer, apoptosis, Zerumbone, *Zingiber zerumbet*.

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The Proteome Analysis of Human Hepatocellular Carcinoma Cell Line HepG2 in Response to *Catharanthus roseus*-silver Nanoparticles: A Preliminary Study

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The incidence of human hepatocellular carcinoma (HCC) is increasing with alarmingly mortality rate. Despite the limitations of conventional anticancer treatment, biosynthesised silver nanoparticles (AgNPs) have shown remarkable anticancer activity that potentially applied as an alternative. However, the protein expression of these *C. roseus*-AgNPs treated cancer cells remain unexplored. Therefore, a preliminary study was conducted to identify and analyse the differentially expressed proteins in HCC cell line HepG2 treated with *C. roseus*-AgNPs. The HepG2 cell line was treated with 12 µg/mL of *C. roseus*-AgNPs for 24 hours. The proteins extracted from the cells were separated using the sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE). The molecular weight of the proteins were identified by migration distance and cross referred to Expasy:SIB Bioinformatics Resource Portal. A further comparative proteomic approach was performed to identify the novel *C. roseus*-AgNPs-related proteins in HCC. The treated HepG2 cell line showed potential up regulated proteins in comparison to the control. The analysed proteins with approximately 103.0 kDa, 63.0 kDa and 39.0 kDa may be related to carcinogenesis and immunoregulatory activity. The findings obtained would highlight the potential protein as therapeutic and prognostic tools particularly for hepatocellular carcinoma.

Keywords: HepG2, HCC, *C. roseus*-AgNPs, two-dimensional gel electrophoresis, proteome

Construction of Recombinant OTUB1 Knockdown in Breast, Bone and Liver Cancer Cell Lines

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Cancer is one of the leading causes of mortality and morbidity all over the world. Various types of cancer-causing genetic aberrations are well characterized such as mutations, gene amplification, translocation, structural deletion and chromosomal mis-segregation. With the use of modern genomic technologies, we are now beginning to understand the complexity of cancer. The growing understanding of cancer cell biology and tumour progression are gradually leading to better methods for treating the disease. The emergence of genome editing tools offers an alternative solution to combating this disease by disrupting expression of cancer genes. In this study, the current genome editing tool, CRISPR/Cas9, is used to demonstrate its potential in disrupting the expression of OTUB1 gene in breast, bone and liver cancer cells. OTUB1 gene is ubiquitously expressed in human tissues and play an important role in many physiological and pathological processes of human. Overexpression of OTUB1 is also strongly correlated with cancer progression. Transfection of CRISPR/Cas9 nuclease against OTUB1 gene in cancer cells showed a significant knockdown of gene expression. Transfected cells showed a reduction in RNA yield. Analysis of Fluorescence-activated Cell Sorting (FACS) also showed a significant difference in GFP expression in treated cells. These encouraging results will enable us to conduct further investigations on exploring the role of OTUB1 gene in signalling pathways of different types of cancer. These results show that CRISPR/Cas9 can be a promising tool for cancer treatment strategies in the future.

Keywords: CRISPR/Cas9, OTUB1, recombinant, cancer

Prevalence of Hypochromic Microcytic Anaemia in Children Treated in AMDI USM

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Anaemia has been recognized over the years as a global health problem. The commonest types of anaemia in the world are hypochromic microcytic anaemia with the prevalent causes of iron deficiency anaemia (IDA), thalassemia and anaemia of chronic disease (ACD). Although studies concluded that the high incidence of anaemia is due to IDA and thalassemia, majority of the studies done are often small scale and focusing on a certain region. Thus, the study aims to determine the prevalence of hypochromic microcytic anaemia in children age six months to 15 years old treated in AMDI, USM. A cross-sectional retrospective study was conducted among 274 children age six months to 15 years old, treated in AMDI, USM. The data were obtained from Computerized hospital data (CARE2X), Laboratory Information System (LIS) or medical record. Parents of the eligible participants were called for any incomplete data and verbal consents were obtained. Descriptive analysis was conducted to determine the prevalence whereas the relationship between independent variables with types of anaemia were examined using simple logistic regression. The prevalence of anaemia was 22.3%. Among the anaemic children, the predominant morphology form was hypochromic microcytic anaemia (82.0%) followed with normochromic normocytic anaemia (18.0%). IDA was found to be the commonest cause (24%), followed by IDA with concomitant thalassaemia (14%) and thalassaemia alone (8%). In the simple logistic regression analysis, no significant association was found. Prevalence of anaemia was 22.3%, which is considered as moderate public health problem according to WHO. Hypochromic microcytic anaemia was predominant morphology form (82.0%) and IDA was the commonest causes (24.0%). Therefore, we recommend the health authorities to emphasizes on early detection, advice on iron rich nutrition and prompt treatment to reduce the incidence of IDA in children.

Keywords: anaemia, hypochromic microcytic anaemia, IDA, thalassaemia

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Haemoglobins (HBs) Loaded Water Soluble Hyperbranched Polymer for Development of Artificial Oxygen Carrier

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The difficulties regarding demand, supply and storing of blood for therapeutic use transfusion have initiated extensive efforts to develop artificial blood especially red cell substitutes. The history of these hard work includes a complicated mixture business, ethics and scientific field. As time passes towards expiry, RBC membrane loses its structure integrity but the hb molecule remains intact. Free stroma hb is toxic as it can cause kidney toxicity therefore chemical modification is needed for the continuity of hb use. This study involves experimentation using hyperbranched polyglycidol to encapsulate bovine hb and human hb extracted from expired blood donation to produce red cell mimic. Polyglicidol is a hyperbranched polymer possessing around 50 to 60% of dendrimeric structure. No significant decrease of concentration ($p > 0.05$) between free-hb and encapsulated complex for both hbs ($p = 0.109$) shows high encapsulation efficiency with 88.1 and 99.0% average indicating least three hb molecules were entrapped within interior chamber of the polyglycidol. Although average of five oxygen reversibility cycles was not significant ($p > 0.05$) for both encapsulated human hb ($p = 0.109$) and bovine hb ($p = 0.109$), addition of polyglycidol for encapsulation of the hbs prolonged the persistence of oxygen reversibility cycle as compared to only one cycle recorded by the free-hb prior to its complete deactivation. The comparison of encapsulation efficiency ($p = 0.100$) and oxygen reversibility cycles ($p = 0.109$) between encapsulated human hb and bovine hb were not significant ($p > 0.05$) demonstrated the performance of bovine hb was similar to human hb. This suggests that human hb could also be substituted by bovine hb as the latter is easier to obtain. This study utilising hb-polyglycidol system signifies a noteworthy footstep in the progress of red cells substitute production with extended oxygen delivery in the circulation.

Keywords: blood substitute, HBOC, polymer

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Analysis of IRF9 Phosphorylation in Type I Interferon Response

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Interferon regulatory factor 9 (IRF9) is a transcription factor known to be involved in the activation of type I interferon response. Upon binding of type I interferons (i.e. IFN-α/β) to its receptors, IRF9 associates with STAT1 and STAT2 dimer to form the interferon-stimulated gene factor 3 (ISGF3) complex – via the canonical Janus kinase-Signal transducer and activator of transcription (JAK-STAT) pathway – and activates the transcription of antiviral genes. The activation of type I interferon response through the JAK-STAT pathway is regulated by post-translational modifications, most notably phosphorylation on JAKs, STAT1 and STAT2 proteins. The phosphorylation state of IRF9 however, is unknown. Unlike the other eight human IRF members, IRF9 is the only member not known to be phosphorylated. Therefore, we hypothesize that IRF9 is phosphorylated during the type I interferon response and seek to understand its physiological relevance. Two cell lines, HeLa and 2fTGH cells were used. Both cell types were induced with IFN-β and total lysates collected after 24 hours. Phosphoprotein enrichment assay, Phos-Tag™ gel shift assay and phosphatase assay were carried out to determine the phosphorylation state of IRF9 in relation to Type I interferon response. IRF9 was enriched in the phosphoprotein fraction after selective enrichment using phosphoprotein column. Furthermore, the SDS-PAGE migration rate for a portion of IRF9 was reduced with the addition of Phos-Tag™, resulting in observation of doublet band for IRF9. Interestingly, the signal intensity for the slower migrating IRF9 band was reduced with prior treatment with calf intestinal alkaline phosphatase. This was not observed in polyacrylamide gels without Phos-Tag™. Regulation of human IRF9 during type I interferon response is not well understood. Our findings suggested towards IRF9 phosphorylation in type I interferon response. We are currently identifying the phosphorylated site of IRF9 to elucidate the regulatory mechanism and functional importance.

Synthesis and Characterization of PEGylated Glycol Chitosan Polymer for Hydrophobic Drug Delivery

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Chitosan has been widely used in biomedicine and biopharmaceuticals. It is unique due to its reactive amine group which allows chemical modifications to form a wide range of chitosan derivatives. Glycol chitosan (GC) is one of the chitosan derivatives that has hydrophilic ethylene group branch on its sugar backbone. The free amine and hydroxyl groups at the GC backbone have been utilized for further chemical modifications of the polymer to suit the need of intended nanoparticles. The objective of this study is to synthesise and characterise palmitoylated glycol chitosan polymer grafted with polyethylene glycol (PEG) using a stepwise protocol of PEGylation and palmitoylation of the GC. This study was carried out using GC as a starting material. GC was subjected for acid degradation to reduce its molecular weight. The degraded GC was later attached with PEG to form GC-PEG using methoxy polyethylene glycol succinate N-hydroxysuccinimide at either room temperature (RT) or 50ºC reactions. After PEGylation, different ratios of palmitic acid N-hydroxysuccinimide (PNS) were used to form palmitoylated GC-PEG (PGC-PEG). The product of each step was confirmed using proton nuclear magnetic resonance (^{1}H-NMR) and Fourier-transform infrared (FTIR) spectroscopy. Degree of PEGylation and palmitoylation were calculated from the NMR spectra. The degree of PEGylation was 4.2% for the GC that was reacted at 50ºC compared to 3.3% for reaction at RT. The degree of palmitoylation was 60% and 34% when 792 mg and 396 mg of PNS used, respectively. FTIR confirmed the PEGylation of the GC by assessing the attachment of the succinimidyl group to the amino group on the GC via the amide linkage. As a conclusion, the stepwise protocol was able to produce PEGylated GC-based polymer with palmitoylation for the hydrophobic modification of the polymer. The polymer criteria are to be applied in nanoparticle-drug formulation later on in the study.

Keywords: drug delivery, glycol chitosan, PEGylation, palmitoylation

Exploring Adsorption Efficiency of Activated Carbon-Based Magnetic Iron Nanoparticle Prior to The Detection of 2,4-Dichlorophenol in Aqueous Medium Using Uv-Vis Spectrophotometer

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This study investigates the adsorption efficiency of activated carbon-based magnetic iron nanoparticles (Fe_3O_4-AC) towards the removal of 2,4-dichlorophenol using UV-vis spectrophotometer. Adsorbent Fe_3O_4-AC was synthesized and characterized in detail using Fourier transform infrared (FTIR), thermogravimetric analyzer (TGA), scanning electron microscope (SEM), transmission electron microscope (TEM), and Brunauer Emmet Teller (BET) to study their physical and chemical properties. The characterized adsorbent was subjected to various experimental parameters include pH, contact time, adsorbent dosage, initial concentration, and temperature. Results obtained via optimization was further used in kinetic, isotherm and thermodynamic analysis. This work was then applied in real industrial wastewater samples. Based on the results obtained in this study, it can be concluded that the adsorbent Fe_3O_4-AC synthesized in this study act as an excellent adsorbent towards phenolic compounds and can be applied in real wastewater mediums.

Keywords: magnetic iron particles, activated carbon, 2,4-dichlorophenol, UV-vis spectrophotometer, adsorption.

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Sequencing Profile of Long Non-Coding RNA in Colorectal Cancer

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Long non-coding RNA (lncRNA) is a class of non-coding RNAs with length of more than 200 nucleotides and are not translated into a protein due to lack of protein-coding capacity. LncRNAs are aberrantly expressed in cancers and involved in many biological behaviours such as proliferation, invasion and metastasis. Colorectal cancer (CRC) is one of the most common malignant cancers with high incidence and mortality. Our aim is to investigate and profile the lncRNAs expression in CRC with the ultimate goal to elucidate their potential roles in CRC pathogenesis. Patients of different CRC clinical stages were enrolled in this study at the Department of Surgery, The First Affiliated Hospital of Xinxiang Medical University (XXMU), where several tumour/non-tumorous tissues were collected. The human ethical approval was obtained from both XXMU and Universiti Sains Malaysia's Human Ethics Committee. The lncRNAs were sequenced on a Hi-seq platform and the expression profile of lncRNAs was established. A total of 294 lncRNAs have significant differential expression in CRC tissues compared with normal tissues, in which, 146 were down-regulated and 148 were up-regulated in tumour tissues. Six down-regulated lncRNAs, five up-regulated lncRNAs and three additional lncRNAs were selected and the expression was validated in 10 patients' samples by quantitative real time PCR analysis. The expression of these lncRNAs was further validated in normal colon cell line (NCM460D) and 4 CRC cell lines (HCT116, HT-29, Caco-2, SW1463). Two potential lncRNA have been identified, i.e. lncRNA 1 and lncRNA 2. LncRNA1 showed down-regulated expression in all CRC tissues and cell lines (p<0.05) while lncRNA 2 showed up-regulation in most of CRC tissues and cell lines as compared to that of the normal paired samples.

Key words: colorectal cancer, long non-coding RNA, Hi-Seq, expression profile.

Dosimetric Analysis of Effect Of Bladder Volume on Organs at Risk Using The Vienna Applicator in High-Dose-Rate Intracavitary Brachytherapy in Cervical Cancer - A Single Institutional Experience

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The purpose of this study was to establish a dosimetric correlation between the bladder volume and its effects on the organs at risk (OARs) (bladder, rectum and sigmoid) during computed tomography (CT)-guided high-dose-rate (HDR) intracavitary brachytherapy in cervical cancer, and to find optimized bladder volume to reduce the dose to OARs. Fifteen intracavitary applications of cervical cervix treated with external beam followed by CT-based HDR intracavitary brachytherapy (the Vienna applicator consist of a tandem and a ring with 7 interstitial catheters insertion) at our institute from June 2015 to April 2018 were studied. Contouring of high-risk clinical target volume (HRCTV) and OARs based on CT images were done on Oncentra MasterPlan Treatment Planning System. The bladder volume at contouring procedure was noted and was correlated with various 3D dose volume histogram (DVH) parameters including 0.1 cc, 1 cc and 2 cc OARs doses. The most exposed 2 cc of bladder (D_{2cc}) increases by increasing the volume of bladder up to volume of 170 cc and then starts decreasing. The highest bladder dose observed was in the bladder volume, range 120-170 cc. The minimum doses were recorded when bladder volume was, in range 0-80 cc. D_{2cc} of rectum and sigmoid follow a similar as that of the bladder. The highest rectum and sigmoid doses observed were in the bladder volume, range 120-170 cc but the minimum doses were recorded when bladder volume was >170 cc. As conclusion, there are relationship between the volume of the OARs and the dose received by them. The mean D_{2cc} of sigmoid was significantly affected by the different bladder volume but not significantly affected the bladder and rectum doses. A bladder volume about 120 cm^3 or less proved better for achieving the prescribed dose limit for bladder, rectum and sigmoid. In this study also showed that, with a distended bladder volume more than 170 cm^3 the dose to OARs can be reduced to the permitted level. However, further evaluation and validation are necessary.

Keywords: organ at risk doses, intracavitary brachytherapy, cervical cancer.

Validation of Breast Cancer Induced to Bone Model Using ^{99m}Tc-MDP

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Metastasis is a complex process by which tumour cells escape from the primary site and form a new lesion in other organs. It is a common phenomenon of malignant disease where bone is the frequent metastatic site and the effect of bone metastasis to other organs are poorly understood. Bone scan using 99m-Techetium-Methylenediphosphate (^{99m}Tc-MDP) is used to diagnose bone related pathologies such as osteomyelitis, bone metastases and occult fracture. The uptake is bone specific however non osseous structure uptake is an indicator of tissue abnormalities. This study is aimed to validate ^{99m}Tc-MDP in breast cancer induced to bone rat model. The rats were divided into two groups. which include Sham (normal) and cancer induced group. For cancer induced group, the left femur was induced with MDA-MB-231, breast cancer cell line. After 21 days, all the rats were subjected to SPECT-CT scan with 1 m Ci^{99m}Tc-MDP injected through tail vein. The model was validated, and cancer induced rats were shown to have kidney uptake of ^{99m}Tc-MDP. Histology shown presence of calcium crystals in the kidney. Our finding suggested that kidney of ^{99m}Tc-MDP uptake is due to the calcium crystal presence in the kidney. This condition is termed as nephrocalcinosis. Calcium presence in the kidney was proposed as an indicator of cancer progression. However, further study needs to be done to confirm this mechanism.

Keywords: SPECT-CT, Metastasis

The Regulation of Macrophage Foam Cell Formation by Murine Norovirus-3 and Peroxisome Proliferator-activated Receptor γ Ligands

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Atherosclerosis is the principal underlying cause of death due to heart diseases globally and the formation of macrophage foam cells is the hallmark of early stage of atherosclerosis. Virus infections have been reported to affect the development of atherosclerosis. Murine norovirus (MNV) replicates efficiently in macrophages and dendritic cells. The strain MNV-3 establishes persistent infection in mice which makes it an attractive strain for elucidating the effect of norovirus infection in atherogenesis development as a model system. Peroxisome proliferator-activated receptor γ (PPARγ) is expressed in macrophages and numerous researches have demonstrated the anti-atherosclerosis effects of PPARγ ligands. In this study, MNV-3 and PPARγ ligands namely prostaglandin (15d-PGJ2) and ciglitazone were used to study their regulation in the foam cell formation involving RAW 264.7 macrophages. MNV-3 infection was found to decrease the total cholesterol content of oxLDL treated and untreated RAW 264.7. Interestingly, MNV-3 and both PPARγ ligands synergically decreased the total cholesterol content in oxLDL treated RAW 264.7. We also found that 15d-PGJ2 and ciglitazone affected MNV-3 replication by increasing and decreasing the viral titer respectively. We also measured the RNA expression of selected genes semi-quantitatively and found an increased expression of T-bet was primarily determined by the presence of oxLDL. Furthermore, treatment of RAW 264.7 cells with 15d-PGJ2, MNV-3, MNV-3+15d-PGJ2, and MNV-3+ciglitazone has been found to diminish the RNA expression of PPARγ in the presence and absence of input oxLDL. Additionally, a correlation between the decrement of PPARγ RNA expression and the reduction of total cholesterol content was observed in the involved treatments. Altogether, this study revealed the roles of MNV-3 and PPARγ ligands in the formation of macrophage foam cells.

Keywords: atherosclerosis, foam cells, macrophage, MNV, norovirus, PPARγ, PPARγ ligands

Tocotrienol Supplementation for Pain Relief in A Rat Model of Breast Cancer-Induced Bone Pain

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Cancer-induced bone pain can occur either from a primary bone cancer or from a cancer that has metastasized to the bone. Pain generally come along from cancer patients with bone metastasis due to excessive skeletal-related complications such as pathological fractures, life-threatening hypercalcemia and nerve compression syndrome. Search for new therapeutics options is important to control the pain and provide effective and fast relief to patients. Tocotrienol rich fraction is the new antioxidant which might play an important role as an adjuvant treatment. This study aimed to evaluate the role of Tocotrienol Rich Fraction in reducing pain in a rat model of breast cancer-induced bone pain. The rats were randomly divided into four groups of eight rats according to the experimental design. Cell line of MDA-MB-231 were induced into the left femur of the rats of three groups which includes Control, Tocotrineol Rich Fraction, and Zoledronic Acid groups, whereas the Sham group was induced with culture media only. Pain assessment tests were carried out every four days and body weight were recorded every seven days to evaluate any pain and discomfort from the rodents. After 20 days, all the rats were subjected to SPECT-CT scan to validate the model and determine any abnormal imaging uptake using radionucleotide tracer 99mTc-MDP. Tocotrienol rich fraction shown a promising effect in reducing the pain. This finding suggest that Tocotrienol rich fraction has potential to be used as supplementation for pain relief. However, further study on mechanism of action will need to be done.

Keywords: cancer-induced bone pain, Tocotrienol Rich Fraction, in-vivo SPECT/CT imaging

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Elucidation of Circrna Roles and Functions in Colorectal Cancer Pathogenesis

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Circular RNAs (circRNAs) are the special endogenous non-coding RNAs (ncRNAs) molecules, A closed loop structure without 5' to 3' polarity and polyadenylated tail. However, little is known about circRNA and its relationship with colorectal cancer (CRC). CRC is the third most commonly diagnosed malignancy and the fourth leading cause of cancer-related deaths in the world. Its global burden is expected to increase by 60% to more than 2.2 million new cases and 1.1 million deaths by 2030. It is essential to identify some new molecular markers to raise the efficiency of tumor diagnosis. circRNA act as natural miRNA sponges and so compete with other RNAs for binding to miRNAs, circRNA also can bind proteins (RBPs) for its mRNA targets. circRNA has stable expression as they are not affected by RNA enzymes, and they are not easily degraded. In our study, differentially expressed circular RNAs were detected using circular RNA sequencing in paired tumor and adjacent normal tissues from 3 CRC patients. Expression levels of selected circular RNAs were measured by qPCR in 10 paired colorectal cancer samples and 6 kind of CRC cell lines for further validation. Our results indicated that there were 59 down-regulated and 20 up-regulated circular RNAs in colorectal cancer tissues compared with normal tissues($p<0.05$). We also first demonstrated that the expression levels of hsa_circRNA_037236 ($p < 0.05$) and hsa_circRNA_029532 ($p < 0.05$) were significantly increasing in CRC cell lines than in normal human colon mucosal epithelial cell line; the expression levels of hsa_circRNA_007667 ($p < 0.01$) was significantly lower in colorectal cancer than in normal tissues and in CRC cell lines than in normal human colon mucosal epithelial cell line.

Keywords: circular RNA (circRNA), colorectal cancer, sequencing, qPCR, validation.

The Anti-Cancer Effect of Vernonia Amygdalina Leaf Extract and Silver Nanoparticles on Kasumi-1 cells

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Vernonia Amygdalina (*VA*) is a traditional West African medicine that has been reported to have a myriad of therapeutic effects, including anti-cancer properties. However, its mechanism in curbing leukemia growth and spread is still not clear. Hence, this study aims to study the efficacy of the anti-cancer properties of *VA* leaf extract and silver nanoparticles on the kasumi cell lines. *VA* leaves were extracted via sequential extraction. Cell viability of treated cells were investigated using MTT assay. The results show that *VA* ethanolic extract and silver nanoparticles reduced Kasumi cells viability in a time- and dose-dependent fashion. The IC_{50} value for VA ethanolic extract and silver nanoparticles at 48h are 15.33 ± 4.62 µg/ml and 6.33 ± 1.53 µg/ml respectively. However, *VA* 50% ethanolic and aqueous extracts showed no significant effect on cell viability. Further research should be done to explore the cell death mode and cell cycle arrest of kasumi cells when treated with *VA* ethanolic extract and *VA* silver nanoparticles.

Keywords: *Vernonia Amygdalina*, leukemic cell, extract, silver nanoparticles

Study on Adsorption Behavior of Modified B-Cyclodextrin Magnetic Nanoparticles Towards The Removal of Phenolic Compounds from Aqueous Samples

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A magnetite coated modified β-cyclodextrin based adsorbent was developed for the removal of phenolic compounds namely bisphenol A, 2,4-diclorophenol and 2,4-dinitrophenol from aqueous samples. The material was characterized using Fourier transform infrared (FTIR), scanning electronic microscope (SEM), transmission electron microscope (TEM). Several parameters influencing the adsorption efficiency of the adsorbent such as pH, contact time, sample volume, amount of sorbent, initial concentration was optimized. Results obtained via optimization were further used in kinetic, isotherm and thermodynamic analysis. This work was further applied for the removal phenolic compounds from environmental samples.

Keywords: adsorption, cyclodextrin, phenolic compounds nanoparticles.

Synthesis of Magnetic Molecularly Imprinted Polymer-Deep Eutectic Solvent as an Adsorbent for The Removal of Naproxen from Aqueous Sample

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Novel magnetic molecularly imprinted polymers-deep eutectic solvent (MMIP-DES) has been successfully synthesised by employing naproxen as a template molecule, methyl acrylate acid (MAA) as a monomer and ethylene glycol dimethacrylate (EDGMA) as a cross linker. The synthesized materials were characterized by fourier transformed infrared spectroscopy (FTIR), scanning electron microscope (SEM) and visible sample magnetometer (VSM). MMIP-DES has showed great removal percentage and adsorption capacity compare to MIP without DES. In addition, these imprinted polymer adsorbents has showed outstanding selectivity and recognition towards target analyte compare to non-imprinted polymer adsorbents, MNIP and MNIP-DES. Therefore, these materials have great potential for efficient removal of naproxen from water samples as alternative to conventional MIP.

Keywords: naproxen**,** magnetic molecular imprinting polymer, deep eutectic solvent, adsorption

A Mobile Augmented Reality Approach for Training in Orthodontics

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Orthodontic education, which currently emphasises a didactic and apprenticeship approach, is facing numerous pedagogical challenges that affect knowledge delivery and instruction. The aim of this study is to discuss the challenges and limiting factors that affect orthodontic training and propose the use of mobile augmented reality (MAR) to create a platform for effective learning, visualisation, deliberate practice, effective feedback, and a personalised learning environment. MAR, with its visually enriched clinical simulations and ubiquitous learning, can effectively reduce cognitive dissonance and improve overall retention and skill gain by students. However, MAR has its limitations, as the technology is still new and limited evidence is available to back up the claims of knowledge and skill gain in the health professional's education. This study also provides future directions for exploring and enabling MAR so that it can become an efficient tool for learning and instruction across all faculties of education.

Keywords: interactive learning, mobile augmented reality, orthodontic education, simulation-based learning, technology-assisted learning

Study Of Different Contrast Administration Protocols For Routine CT Thorax Examination and its Effect on Image Quality and Contrast Enhancement in Two Tertiary Centres

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The objective of this study was to compare the degree of contrast enhancement and image quality using different contrast administration protocols. Data was retrospectively collected from 70 patients from each centre, Group A from Advanced Medical and Dental Institute (IPPT) Universiti Sains Malaysia, and Group B from Hospital Pulau Pinang (HPP), Ministry of Health Malaysia. Group A patients [19 males, 51 females; mean age ± standard deviation (SD) 53.6 ± 11.2 years; mean weight ± SD 54.04 ± 13.77kg] underwent computed tomography (CT) thorax examination using automatic bolus tracking (ABT) with weight-based contrast volume (WBV) administration. As for Group B [24 males, 46 females; mean age ± SD 54.5 ± 13.2 years], the patients underwent this examination using fixed-time delay (FTD) with fixed contrast volume (FV) technique. Quantification of degree of contrast enhancement in different veins and arteries was determined by measuring Hounsfield Unit (HU) values, and rated on 5 point scale (1=very poor, 5=excellent) for qualitative assessment. The mean of enhancement values in Group B were found to be higher than those in Group A (p<0.001). For both group, there was no statistical significant difference for mean of qualitative scores on 5-point scales (p=0.185). A weak correlation was seen between HU values and administered contrast volume (r=0.1152). Overall, FTD with FV protocol was found to yield higher degree of contrast enhancement for routine CT thorax examination. The qualitative assessment showed no significant difference between both protocols even though higher mean grading in CT image quality was given by assessors for ABT with WBV technique.

Keywords: contrast enhancement, image quality, protocols, computed tomography

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Application of CMOS Optical Tracking Camera in Image-Guided Radiotherapy (IGRT)

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Image-guided radiotherapy (IGRT) is a cancer treatment method that incorporates imaging technology to localise the tumour target and to guide the targeted radiation beam during treatment. By providing online patient setup verification and immediate correction before treatment, IGRT offers better treatment outcome and improves the safety of the patients. However, IGRT has difficulty in tracking breathing induced tumour motion in real-time. Over the past decade, several breathing motion management techniques were introduced. Nonetheless, the introduced techniques require either the use of external surrogates or additional x-ray beam, wherein patients would expose to extra radiation during treatment. Therefore, there is a call for a non-invasive imaging system that can track both patient surface and internal movement in real-time. In this study, we proposed the application of fast time-of-flight (ToF) camera in conjunction with kV cone-beam CT to monitor patient breathing motion. ToF camera is a non-invasive 3D imaging device that provides patient surface information; where else, kV cone-beam CT gives the internal view of the tumour target site. In this work, the characteristics of the ToF camera are investigated, and the imaging performance of kV cone-beam CT is evaluated. In characterising the ToF camera, experiments like dark current test, wiggling test and motion tracking test were performed. For the evaluation of kV cone-beam CT system, image quality parameters, such as uniformity, spatial resolution and contrast-to-noise ratio (CNR) are studied. Furthermore, to correspond to the patient breathing cycle, imaging protocols of kV cone-beam CT system are investigated, and a fast imaging protocol for head and neck region is developed. In the last part of the work, the motion tracking test was performed by using ToF camera together with kV cone-beam CT. With the proposed technique, simulated patient breathing motion is monitored, and an internal transverse planar image is generated for verification purpose.

Keywords: time-of-flight, kV cone-beam CT, dynamic motion tracking, image quality

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Automated Decision Model for Tractography Pipeline Selection

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Diffusion refers to the random, microscopic movement of water and other small molecules due to thermal collisions. This phenomenon is also present in the human brain. Additionally, due to the arrangement of fibers in the brain tissue, a directional dependence is introduced into this motion, as water molecules encounter less resistance along the fibers than in their perpendicular orientation. A specialised sequence of MRI known as diffusion MRI (dMRI) can be employed to capture this movement of water molecules. Orientations of entire fibre can be assessed by measuring the dMRI signal for each imaging voxel along several non‐collinear orientations. These local fiber orientations can then be pieced together to generate long‐range pathways connecting distant regions of the brain. This process is often referred to as fiber tracking or fiber tractography. These pathways form the neural substrate for information transfer between distinct brain regions and are therefore significant to our understanding of brain function. Generating a diffusion tractograph from raw MRI data involves multiple layers of processes. Each set of processes that produces a particular analysis is called a pipeline. An extensive collection of software tools have been developed over the years for each layer of tractograph generation, giving researchers the freedom to choose the tools of their preference for different processes. However, this has resulted in the establishment of various pipelines aimed towards the same task, and depending upon an analysis, one pipeline may be more suitable in terms of time efficiency or accuracy than the other. However, there is no automated protocol available to evaluate which pipeline is better for a particular analysis. Our study aims to address this issue by designing an automated decision model, which will help the researchers to choose a pipeline best suited for a particular analysis.

Keywords: Diffusion Tensor Imaging (DTI), tractography, pipeline, workflows, fuzzy logic.

Artefact Index Evaluation of Different Sinogram Interpolation Techniques for Metal Artefact Correction in CT Imaging

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Metal-induced artefacts may degrade image quality and lead to misinterpretation in diagnostic radiology especially in computed tomography (CT) images. The aim of this study was to evaluate the artefact index on corrected CT images using two different sinogram interpolation (SI) methods for metal artefact correction induced by metal hardware. A phantom with metal hardware was scanned with CT scanner to simulate the metal-induced artefacts of different degree of severity. The artefact correction was performed on the image raw data known as sinogram. The metal region in the sinogram was delineated and removed by dual-thresholding technique. Two sinogram interpolation methods which were cubic spline and Laplace interpolation were used to replace the missing part of metal trace on the sinogram. Both SI methods were applied to the selected phantom images of different artefact severity. The effectiveness of both SI methods were evaluated by comparing the artefact index. The findings showed Laplace interpolation method was better as compared to cubic spline interpolation. Laplace technique produced a lower mean artefact index compared to cubic spline technique. It can be concluded that the Laplace interpolation works more effectively and was successfully replaced all the missing sinogram data compared to cubic spline technique especially for a more complicated thresholded sinogram.

Keywords: computed tomography, artefacts, sinogram interpolation, metal artefact reduction, image processing

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Assessment of Image Distortion in Dental Cone-Beam Computed Tomography (CBCT) Imaging: A Phantom Study

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This study aimed to assess image distortion due to beam misalignment for dental cone-beam computed tomography (CBCT) system using phantom study. A ball phantom was scanned using Planmeca ProMax 3D Mid CBCT unit (Planmeca, Helsinki, Finland). The exposure factors used were based on default setting (68 kV, 8 mA and patient size M). Three different measurement were performed on the ball phantom images such as distance measurement between the centre of the middle ball and rear middle ball, distance measurement from the centre of the middle ball to the tenth ball (both left and right), and measurement of both vertical and horizontal distance of any four balls. The findings showed that the measured distance between middle ball and rear middle ball were below the acceptable level (<1.6 mm). Only one measurement exceeded the acceptable level (75%). The measured distances from middle ball to tenth ball of both sides were also within the acceptable level (difference ≤ 3.2 mm). Only one measurement exceeded the value by 22%. The vertical and horizontal distance of four selected balls were slightly different by mean value of magnification was 0.96. The beam alignment and patient positioning should be accurately evaluated to avoid image distortion and misdiagnosis in dental CBCT images.

Keywords: cone-beam computed tomography, dental imaging, image quality, quality control

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Role of Saffron (*Crocus sativus*), Pepper (*Piper nigrum*) and Mangosteen Peel (G*arcinia mangostana*) in Treating Alzheimer's Disease and cControlling Aging Process

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterised by cognitive impairment, severe memory loss, behavioural changes and dementia, affecting almost 10 million people worldwide. The symptoms are caused by accumulation of amyloid-β (Aβ) protein and phosphorylation of tau protein leading to death of nerve cells in brain. Consequently, choline acetyltransferase (ChAT) is reduced, affecting the production of a neurotransmitter called acetylcholine (ACh). Enzymes, acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) further break down existing acetylcholine in this region into inactive choline and acetate affecting deterioration in AD patients. Current treatments for AD are administration of acetylcholinesterase (AChE) inhibitors, which blocks the enzymatic hydrolysis of acetylcholine. Agents currently in use clinically have limited efficacy and may produce adverse effects, such as nausea, vomiting, diarrhoea, dizziness, and weight loss. Besides that, amyloid beta (Aβ) peptide is produced from aberration in the proteolytic processing of the amyloid precursor protein (APP). Increased production and accumulation of Aβ peptides leads to the formation of amyloid plaques. This is reported to be neurotoxic and causes cell death. Thus identification of anti Aβ peptides and acetylcholinesterase inhibiting compounds would allow better management of AD. Spices have been used in various forms including flavouring agents, colorants, and preservatives, where some are considered to be able to delay, prevent or treat age-related diseases such as AD. Saffron has been acknowledged as memory enhancing agent, AChE moderator, effective antioxidant, anti-inflammatory, anti-amyloidgenic activities and protective agent against toxicities. Black pepper (*Piper nigrum*) had displayed antimicrobial; anti-inflammatory; antioxidant; lipid peroxidation lowering; oxidative stress reducing and neurodegeneration ameliorating characteristics in AD. Mangosteen fruit (*Garcinia mangostana*) contains ascorbic acid (vitamin C) and phenolic compounds while mangosteen pericarps (peels) contains xanthones and anthocyanins which may play a remarkable role in managing AD and aging. Overall, saffron-pepper-mangosteen peel combination may improve cognitive functions, memory and slow aging process, with reduced adverse effects.