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Name : Assad Ali Faraj Elyagoby
Title : Colon-Specific Delivery Of 5-Fluorouracil From Zinc Pectinate Spheroids Through In Situ Intra-Capsular Ethylcellulose-Pectin Plug Formation
Supervisor : Associate Prof. Dr. Wong Tin Wui (MS)

A study to evaluate the effects of nicotine and simultaneous supplementation of γ-tocotrienol (γ-TCT), one of the four isomers in tocotrienols (TCT), and nicotine, on in vitro and in vivo embryonic development in mice (Mus musculus) had been carried out. Several approaches were undertaken including an investigation on in vitro effects of various doses and durations of nicotine treatment on pre-implantation embryonic development. Results showed that nicotine treatment decreased the number of retrieved embryos, resulted embryo degeneration, delayed embryo cleavage, induced disproportionate size of blastomeres and degraded blastomeres (p<0.05). Moreover, the deleterious impact of nicotine on pre-implantation embryonic development was dose- and treatment duration-dependent with a corresponding increase in plasma malondialdehyde (MDA) concentrations (p<0.05). Based on this finding, the study was further elucidated in terms of examining the dose-related beneficial effects of γ-TCT in nicotine-induced cessation of pre-implantation embryonic development in vitro. Results showed that γ-TCT could prevent the duration- and dose-related

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Name : Yuhania Shaflanie Binti Kamsani
Title : Gamma-Tocotrienol Reverses Nicotine-Induced Oxidatives Stress-Related In Vitro And In Vivo Embryonic Development And Pregnancy Outcome In Mice
Supervisor : Prof. Dr. Mohd Hamim Rajikin (MS) Prof. Dr. Amar Chatterjee (CS) Assoc. Prof. Dr. Nor Ashikin Mohd Noor Khan (CS) Assoc. Prof. Dr. Nuraliza Abd Satar (CS)

Conventional fluid-bed and immersion film coating of hydrophilic zinc pectinate spheroids using ethylcellulose-pectin mixture is met with fast drug release due to hydrophobic ethylcellulose coat detachment. This study explored in situ intra-capsular spheroid coating for colon-specific delivery of 5-fluorouracil. The solid coating powder was constituted of ethylcellulose and pectin in weight ratios of 11:0 to 2:9. Its weight ratio to spheroids was varied between 2:3 and 3:2. Delayed 5-fluorouracil release was obtained when the weight ratio of ethylcellulose and pectin in coating powder was kept at 8:3, and weight ratio of solid coating powder to spheroids was kept at 3:2 with particle size of ethylcellulose reduced to 22 μm. In situ intra-capsular wetting of pectin coat by dissolution medium resulted in the formation of ethylcellulose plug interconnecting with spheroids through the binding action of pectin. The majority of drug was released in the colon
region and complete drug release was obtained through digestion of core spheroids by pectinase. Through in vivo pharmacokinetic and pharmacodynamic studies, the intra-capsular coated spheroids were found to be able to reduce the drug bioavailability, enhance its accumulation at colon and reduce both number and size of tumor through reforming the tubular epithelium with basement membrane and restricting the expression of cancer from adenoma to adenocarcinoma. Given a dosage regimen of 15 mg/kg/day for 5 days in rats, the intra-capsular coated spheroids also eliminated the formation of aberrant crypt foci which represented a putative preneoplastic lesion in colon cancer, unlike other treatment modes. Inferring hundred-and-twelve cases and a hundred-and-nineteen controls were successfully recruited and analyzed for the selected SNPs and analytes. Cross tabulation analyses and logistic regression were performed in four different models. Genetic analyses showed that APOE ε4, APOE rs429358, ABCA7 rs3764650, MS4A4E rs670139, MS4A6A rs610932, and CD2AP rs9349407 were statistically significantly associated with AD risk. The distribution of all selected SNPs was also determined after stratifying all samples by the presence of APOE ε4 copy. In the stratified samples, statistically significantly different values were observed only in subjects without APOE ε4 copy for ABCA7 rs3764650 and MS4A4E rs670139. The AD risk of a person with GG genotype for ABCA7 rs3764650 is increased to around 3.7-fold in model I and 5.2-fold in model III. Whereas, the AD risk of a person with AA genotype for MS4A4E rs670139 is increased to around 3.3-fold in model I and III. The mean tHcy levels were statistically significantly higher in cases than in controls while the mean serum holotranscobalamin (holoTC) levels were statistically significantly lower in cases than in controls. The logistic regression analysis showed that the APOE rs429358 is the main predictor variable. Other significant predictor variables were age at assessment, social class, holoTC, ABCA7 rs3764650, MS4A6A rs610932, folate and LDL. The combination of them significantly predicted 35.8% of variance in the model. The developed method will enable researchers to study AD-related SNPs using an inexpensive method. Our findings show that the significant SNPs may influence the AD risk in the population. It is plausible that the effect of other SNPs on AD risk is specific to certain ethnic group or that effect is not large enough to be identified reliably by a cohort of our size. To the best of our knowledge, this is the first study aimed to determine the potential contribution of the SNPs to AD in a Malaysian population.

deterioration of pre-implantation embryo quality when supplemented simultaneously with nicotine. Moreover, γ-TCT of 60 mg/kg bw/day was found to be the optimal effective dose in lowering plasma levels of MDA during pre-implantation embryo development (p<0.05). Findings of in vitro study were applied in in vivo approach to evaluate the effect of simultaneous supplementation of γ-TCT with nicotine on embryo development, blastocyst implantation, foetal growth, length of gestation, foetal outcome and survival rate of the neonates. Results showed that nicotine impaired post-implantation embryo growth and development (p<0.05). Pregnancy outcome and survival of the neonates were also reduced (p<0.05). The rise in oxidant levels reduced the enzymatic antioxidant defense system (p<0.05). Pregnancy-related levels of progesterone (P₄) and oestrogen (E₂) were also significantly affected (p<0.05). Through combating nicotine-induced oxidative stress, γ-TCT was able to sustain the physiological/normal sequence of blastocyst implantation, foetal growth, pregnancy outcome and survival of the neonates. Moreover, maintenance of pregnancy until term possibly resulted from sustaining the levels of plasma P₄ and E₂ as evident in normal pregnancy. In conclusion, γ-TCT could be used to minimize nicotine-induced oxidative stress-related deterioration of pre- and post-implantation embryo development, intrauterine foetal growth, pregnancy outcome and survival of the neonates.