Aim: The aim of this study is to build a quantitative structure-property relationship (QSPR) of 66 thiazolidin-4-one derivatives in order to predict their log P.

Introduction: Performing computational drug design is an important step for their synthesis and properties characterization. In this work, quantitative structure-property relationship (QSPR) of 66 thiazolidin-4-one derivatives was examined in order to predict their logP which is the most commonly used measure of lipophilicity in chemical molecules. These group of compounds act as non-nucleoside reversed transcriptase inhibitors of HIV.

Methods: Two different quantum mechanics approaches including HF and DFT were applied for energy minimization of structures and different classes of molecular descriptors including quantum chemical descriptors were generated for prediction of their LogP. Numbers of descriptors which showed high correlation with each other were removed by MATLAB software. The model between structures and their LogP was built for both methods with performing Multiple Linear Regression (MLR) in Spss package.

Results: Statistical results and application of developed model to the test set demonstrates that the DFT model is reliable with good predictive accuracy. (R2cal = 0.90, R2cv = 0.88) The lack of significant difference between the original and modeled values of logP reveals the validity of the built model which was built with 2D and 3D descriptors. The coefficients of model are statistically significant.

Conclusion: QSPR models can be used to predict molecular properties such as LogP. That will be beneficial in drug design processes. In this research, MLR model was built in order to correlate structure of 66 compounds with their LogP. Molecules that were optimized by DFT method showed better correlation than HF method that indicates the accuracy of the built model with 2D and 3D descriptors.

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Epigenetic modifications as targets to new therapies for Chronic Lymphocytic leukaemia – A preliminary study


1 Department of Chemistry, University of Aveiro, Portugal
2 Laboratory of Oncobiology and Hematology (LOH), University Clinic of Hematology and Applied Molecular Biology, FMUC, Portugal
3 Center for Neuroscience and Cell Biology, IBBI, University of Coimbra, Portugal
4 CIMAGO - Center of Investigation on Environment Genetics and Oncobiology, Faculty of Medicine, University of Coimbra, Portugal
5 Laboratory of Cytogenetics and Genomics (LCG), Faculty of Medicine, University of Coimbra, Portugal
6 Clinical Hematology Service, University Hospital of Coimbra, Portugal

E-mail address: beatriz.ribau@ua.pt

(B. Ribau).

Aim: This study aimed to clarify the involvement of epigenetic modifications in chronic lymphocytic leukaemia development and analyse the therapeutic potential of epigenetic modulators.

Introduction: CLL is the most common type of leukaemia found in adults and is an extremely variable and heterogeneous disease. The CLL aetiology is unknown and its natural history is heterogeneous. However, epigenetic modifications may play an important role in CLL.

Methods: This study enrolled 18 CLL and 7 controls. To perform primary CLL cultures, peripheral blood mononuclear cells from CLL patients were isolated using ficoll gradient and incubated with the hypomethylants, Azacytidine and Decitabine, and decacylase inhibitors, Panobinostat and Vorinostat, in monotherapy (single dose and daily administration) and in combination for 24h/48h. The cytotoxic/cytostatic effect of drugs was evaluated by fluorometric microculture cytotoxicity assay (FMCA). Cell death and cell cycle were determined by flow cytometry using Annexin V and PI/RNAs, respectively. CD5 and CD19 antibodies were used to identify normal (CD5−/CD19+) and neoplastic cells (CD5+/CD19+). Methylation pattern was determined by MS-MLPA. Data were analysed using univariate approaches.

Results: Preliminary results show that patients appear to be more sensitive to Azacytidine and Vorinostat than Decitabine and Panobinostat, on single dose administration. Combination of Panobinostat with Azacytidine and Decitabine induced higher cytotoxicity than single dose. For all drugs, daily administration schedule reduced more effectively cell viability/proliferation than the same doses in single administration. These drugs induced cell death mainly by apoptosis with specificity to neoplastic cells. Moreover, CLL patients had a significant higher methylation frequency of PAX5 (70%), KLLN (80%), WT1 (100%), THBS1 (90%) and GATA5 (90%) gene promoters when compared with controls (all genes demethylated, except MSH6). Furthermore, all CLL patients had at least one methylated gene.

Conclusion: The preliminary results suggest that methylation of tumour suppressor genes is a common event in CLL patients and that epigenetic modulators induce a cytotoxic effect, reducing cell viability/proliferation, in a time- and dose-dependent manner. Therefore, these results are promising and encourage further studies in CLL.

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PS191

Imaging features of brain metastases from testicular cancer

Ana Filipa Pinto, Susana Maria Silva, Eduarda Carneiro, Diana Ferreira, Joaquina Maurício, Mavilde Arantes

1 Faculty of Medicine of the University of Porto, 4200-319 Porto, Portugal
2 Unit of Anatomy, Department of Biomedicine, Faculty of Medicine of the University of Porto, 4200-319 Porto, Portugal
3 Center for Health Technology and Services Research (CINTESIS), 4200–450 Porto, Portugal
4 Division of Neuroradiology, Radiology Service, Portuguese Institute of Oncology, Porto, Portugal
5 Medical Oncology Service, Portuguese Institute of Oncology, Porto, Portugal

E-mail address: anafilipapinto95@gmail.com

(A.F. Pinto).

Aim: Our study evaluated the incidence, imaging characteristics, and prognosis of brain metastases originating from primary testicular tumors.

Introduction: Approximately 95% of testicular tumors are testicular germ cell tumors (TGCT). Sertoli cell tumors are rare non-germ cell origin tumors and account for less than 1% of testicular cancer. Brain metastases from germ cell tumors are very uncommon, occurring in less than 2–3% of patients. In testicular cell cancer, it is estimated that the incidence of brain metastases is 1–2% in all TGCT, whereas in advanced stages of TGCT the incidence rises to about 10–15%.

Methods: Case records of testicular tumors patients within the IPO Porto data base from 2006 to 2015 were reviewed to identify patients with testicular tumors and evidence of brain metastases.

Results: 368 patients with testicular tumors were identified, with only four having evidence of brain metastases.