Med Chem (Los Angeles) 2017, 7:4 (Suppl)
DOI:10.4172/2161-0444-C1-031

Quadruplex DNA stabilizing agents as potential anti-cancer therapeutics

Mrinalkanti Kundu
TCG Lifesciences Pvt. Ltd., India

Over 100 cancers affect human, as per the World Cancer Report, ~14 million new cases of cancer occurred globally resulting ~15% of deaths in 2012. Towards our goal in improving the quality of life for the people suffering from cancer, we are investigating on the identification of small drug-like compounds as potential G-quadruplex (G4s) binders to treat this disease. DNA integrity is critical for proper cellular function and proliferation and has played a key role as successful molecular target for many of the drugs that have been used for decades. Compounds that target DNA are some of the most effective agents in clinical use and produced increase in cancer patients' survival but, they are extremely toxic. Consequently, much effort has been put into finding agents that are more selective and thus presumably will have lesser side effects. Targeting non-canonical DNA secondary structures such as G4s is now considered as an attractive approach toward drug intervention in anti-cancer therapy and thus, significant research is in progress targeting G4 DNAs with small molecules hoping to inhibit cancer growth. We report the design, synthesis of novel small molecules and their evaluation as G4s stabilizing agents. Efficiency of these synthetic compounds was performed to assess the quadruplex binding affinity by using various biophysical and biochemical studies. For the lead compound/s, the binding mode was explained by modeling studies and their *in-vitro* cell growth inhibition was also tested. Finally, drug-likeness of the selected compounds was evaluated for liver microsomal stability, aqueous solubility, CYP inhibition studies.

mrinal.kundu@tcgls.com

Isoconversional approach for non-isothermal decomposition of un-irradiated and photon-irradiated 5-fluorouracil

Refaat M Mahfouz, Hala Sh Mohamed and **Abdel Rahman A Dahy**
Assiut University, Egypt

Kinetic analysis for the non-isothermal decomposition of un-irradiated and photon-beam-irradiated 5-fluorouracil (5-FU) as anti-cancer drug, was carried out in static air and nitrogen atmospheres. Thermal decomposition of 5-FU, proceeds in two steps. One minor step in the range of (270-280^{o}C) followed by the major step in the temperature range of (285-360^{o}C). The non-isothermal data for un-irradiated and photon-irradiated 5-FU, were analyzed using linear and non-linear Vyazovkin (VYZ) isoconversional methods. The results of the application of these free models on the present kinetic data showed quite dependency of the activation energy on the extent of conversion. The results confirm the complexity of the decomposition of 5-FU and more than one reaction mechanism are involved in the process. In the low conversion range of fraction decomposed , the decomposition is best described by diffusion model, D3. At higher values of decomposition, the nucleation mechanism, A4, gave the best fits to the experimental data. The decomposition path was investigated by intrinsic reaction coordinate (IRC) at the B3LYP/6-311++G(d, p) level of DFT. Two transition states were involved in the process by hemolytic rupture of N−H bond and ring secession, respectively.

rmhfouz@science.au.edu.eg