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Targeting oncogenic transcription factors for cancer treatment

Prof. Gautam Sethi
National University of Singapore, Singapore

Email: phcgs@nus.edu.sg

Abstract:

Signal Transducers and Activators of Transcription (STATs) comprise an important class of transcription factors that have been implicated in a wide variety of essential cellular functions related to proliferation, survival, and angiogenesis. Among various STAT members, STAT3 is frequently overexpressed in tumor cells as well as tissue samples, and regulates the expression of numerous oncogenic genes controlling the growth and metastasis of tumor cells. I will briefly discuss the importance of STAT3 as a potential target for prostate cancer therapy and also provide novel insights into various classes of existing pharmacological inhibitors of this transcription factor that can be potentially developed as anti-cancer drugs.

Biography :

After completion of his postdoctoral training at University of Texas MD Anderson Cancer Center, Dr. Gautam Sethi joined Department of Pharmacology, Yong Loo Lin School of Medicine, National University of Singapore in 2008 as an Assistant Professor and was promoted to Associate Professor in 2015. The focus of his research over the past few years has been to elucidate the mechanism (s) of activation of oncogenic transcription factors such as NF-kB/STAT3 by carcinogens and inflammatory agents and the identification of novel inhibitors of these proteins for prevention of and therapy for cancer. The findings of his research work have so far resulted in more than two hundred scientific publications in high impact factor peer reviewed journals (with h index = 71) and several international awards. He currently serves as an Academic Editor for PLOS, editorial board member of Scientific Reports, Pharmacological Research, BMC Cancer, Frontiers in Pharmacology, Frontiers in Oncology, Journal of Natural Products in Cancer Prevention and Therapy, and ad-hoc reviewer for several other prestigious international journals.

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The awesome role of Herbal Nutraceuticals against hazards of radiation therapy

Sohair Aly Hassan*[1], El Sherbiny M[1], Amani N. Hashim[2]

[1]Therapeutic chemistry Dept. / National Research Center, (NRC) Cairo/ Egypt
[2]Phytochemistry and plant Systematics Dept.(NRC), Cairo /Egypt

Email: sohaireslamaya@hotmail.com

Abstract:

Plants are rich sources of anti-oxidants which mainly attribut-ed to its components. Rosma-rinus officinalis L and Tamarixaphylla are among herbal plants, with a long histo-ry of medicinal and culinary use. The modifying influence of leaves extract of both herbs were studied in experimental albino rats. Selected doses were chosen as radio protec-tors against Gamma [γ] radia-tion hazards. The experimental Westar rats were exposed to 5 Gry for 15 min before and after treatment with rosemary and tamarix extracts in a dose of 100 mg/kg/ b/ wt of each re-spectively. The treated animals were autopsied for collection of blood serum at days 1, and 15 post-irradiation. Results: A de-crease in the hematological pa-rameters and Glutathione level was registered in the positive irradiated control group. A re-covery pattern were recorded in the pre and after treated groups. The whole hematologi-cal parameters were ameliorat-ed back to the normal by day 15; as a significant elevation was achieved with groups treated with rosemary and tamarix extracts compared to irradiated one. An increment in the level of lipid peroxidation above normal was noted in se-rum of irradiated rats. This in-crement was significantly re-versed upon treatment by rosemary and tamarix extracts. Moreover interlukin 6 levels were highly modified in the treated groups. The whole re-sults were confirmed Histologi-cally by the improvement seen in the (PCNA) (proliferating cell nuclear antigen)level anti-gen.Conclusion:Considering these biochemical and histolog-ical results, the present study suggests the significant im-portance for both herbs with the superior role of rose marry as a magnificent radio modifier herb.

Keywords:

Tamarix aphylla, gamma radiation, antioxidative ef-fect, PCNA (proliferating cell nuclear antigen).

References:

Rašković A, Milanović I, Pavlović N, Ćebović T, Vukmirović S, Mikov M. Antioxidant activity of rosemary(Rosmarinusofficinalis L.) essential oil and its hepatoprotective potential. BMC Com-plement Altern Med 2014Jul 7;14(1):225.

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Best-selling small-molecule drug: Discovery of Eliquis®/ Apixaban leading to Chan-Lam Coupling Reaction and First Rational Use of Halogen Bonding in Drug Design

Patrick Y. S. Lam

Baruch S. Blumberg Instititue, Doylestown, PA18902, US

Email: Patrick.ys.lam@gmail.com

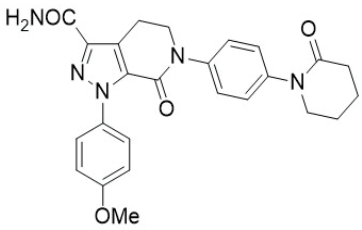
Abstract:

Thrombosis is the leading cause of death in developed countries. There is a significant need for novel antithrombotics with an im-proved safety profile to replace Warfarin which has been in use for ~60 years and has significant bleeding issues. We at Bristol-Myers Squibb/DuPont had discovered a nov-el class of potent, selective and orally bioa-vailable Factor Xa inhibitors culminating in Eliquis®/Apixaban. Eliquis® is currently the best-selling small-molecule drug with annual sales of ~$10B.

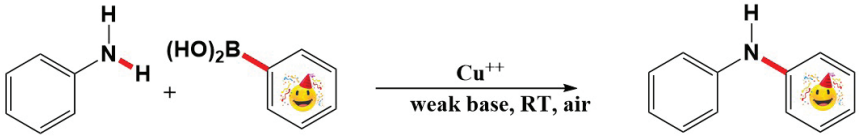
During the optimization process, we have also discovered the powerful Chan-Lam Coupling reaction of copper promoted C-X bond cross-coupling via boronic acids, a complementary reaction to the Nobel prize Suzuki-Miyaura C-C bond Coupling reaction. C-L reaction is currently used in manufactur-ing of an antipsychotic drug.

In addition, at the molecular recognition fron-tier, we have pioneered the first rational use of halogen bonding in structure-based drug design.

A. Eliquis®/Apixaban

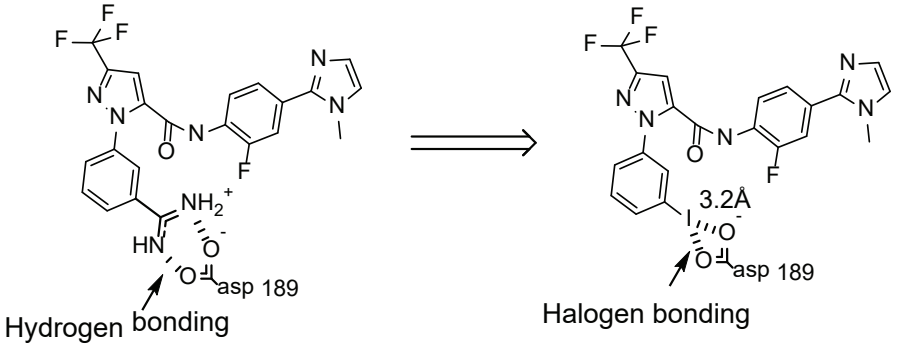


B. Chan-Lam Coupling Reaction



including
O, S, P, Se, Te, C,
F, Cl, Br, I, H, At bonds

C. First rational use of halogen bonding in drug design



Keywords:

Factor Xa inhibitors, Eliquis®, apixaban, structure-based drug design, Chan-Lam reac-tion, halogn bonding.

References:

1. Discovery of 1-(4-Methoxyphenyl)-7-oxo-6-(4-(2-oxopiperidin-1-yl)phenyl)-4,5,6,7-tetrahydro- 1H-pyrazolo[3,4-c]pyridine-3-carboxamide (Apixaban, BMS-562247), a Highly Potent, Se-lective, Efficacious, and Orally Bioavailable Inhibitor of Blood Coagulation Factor Xa." Pin-to, D. J. P.; Orwat, M. J.; Koch, S.; Rossi, K. A.; Alexander, R. S.; Smallwood, A.; Wong, P. C.; Rendina, A. R.; Luettgen, J. M.; Knabb, R. M.; He, K.; Xin, B.; Wexler, R. R.; Lam, P. Y. S.. J. Med. Chem. 2007, 50, 5339-5356.
2. "Copper-promoted Carbon-Heteroatom bond cross-coupling with boronic acids and deriva-tives". Qiao, J. X.; Lam, P. Y. S. Syn. 2011, 829-856.
3. a. "Halogen bonding- a world parallel to hydro-gen-bonding" Symposium in Organic Division, #58, ACS, August 16-20, 2009. Washington DC. Highlighted in C&E News, Sep 21, 2009, p39-42, "…to the best of our knowledge, this is the first successful use of halogen bonding in ra-tional drug design…"; b. JMC, 2013, 1363.

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