

# The Therapeutic and Diagnostic value of Fluorine

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**Abstract - Fluorine has a useful isotope transfer mechanism and enjoys widespread use in the medical field. It is used in fluorinated agents, medical science and the field of steroids. Fluorine infusion with fluoroalkylation is a useful method for the development of new functional and drug components make-up. Fluorine also plays its role as an antibacterial agent and is an effective chemotherapeutic agent for certain types of dangerous growth. 5-fluorouracil plays a vital role in the treatment of cancer. <sup>19</sup>F has the second most sensitive and stable location the active nucleus of NMR.**

## INTRODUCTION

Fluorine has been extensively investigated for its therapeutic and diagnostic powers. The unique properties associated with this unusual feature and its role in drug development/formation has been increasing rapidly. The incorporation of fluorine into a molecule can affect its pharmacokinetic properties structures, metabolic pathways, membrane penetration, internal energy, pKa and integration. <sup>18</sup>F is a useful Positron emitting isotope that finds considerable utility in the clinical field. In the 1950's, fluorine has been used for the first time in the steroid industry. Use of fluorinated agents in medical science is common and electronegative fluorine particle also finds applications in pharmacokinetics, energy and physical science. In 1970s, fluorine substituent was expanded from 2% to 18% in pharmaceutical industries <sup>19</sup>F is a 100% naturally abundant isotope and the second most sensitive and stable NMR-active nucleus. Its absence in almost all of the biological systems make it unique among them and it is commonly used in NMR studies of proteins. To date, only a handful of petroleum products have been left alone. The biosynthesis pathway of 4-fluorothreonine

and fluoroacetate in the bacterium *Streptomyces cattleya* has been significantly investigated and well understood.

## BIOLOGICALLY ACTIVE FLUOROCHEMICALS

Fluorine exposure to organic chemicals has a significant therapeutic effect chemical. When fluorine is incorporated into biologically active compounds, their steric, lipophilic and electronic parameters are altered which results in their increased bioavailability, chemical metabolic and chemical stability as well as their intrinsic activity. Uracil is a compound that contains nitrogen, oxygen, carbon dioxide, and hydrogen. It is one of the most important components of RNA. It is particularly dangerous and is responsible for the development of malignant growth cells. Fluorouracil is a successful chemotherapeutic agent used for the treatment of certain sorts of malignant growth. Another important role of fluorochemicals in improving the quality of human life is the formation of compounds which exhibit anaesthetic properties.

## FLUORINE UTILIZATION IN POSITRON EMISSION

Tomography Imaging (PET) Fluorine-18 is a major isotope used in positron emission tomography (PET). A disadvantage of fluorine-18 is that it cannot act as a true isotopic tracer because in human body, no fluorine containing compound is present. Otherwise, among radio pharmaceuticals <sup>18</sup>F is widely used; it is a major radiopharmaceutical which acts as a glucose transporter in various cells. It is used to indicate various diseases including Alzheimer's disease and epilepsy through FDG-PET. For the treatment of

cancer, two major types of radio pharmaceuticals are used. We reviewed the results for cocaine hydrochloride (40 mg intravenously) in cerebral metabolic glucose levels and submissive reporting to eight polydrug abusers in a blind, placebo-controlled crossover read. Cerebral metabolic rate of glucose levels measured with [fluorine 18] - fluorodeoxyglucose method, using positron emission tomography. introduces white sounds, beep descriptions, and questions about the results below of cocaine or salt. Cocaine produced.

**Fluorinating Agents and C-F Bond Forming Reactions**  
Following the first report of asymmetric fluorination reagents in 1988, there has been a strong focus on providing a preferred introduction of CF bond in the stereo genic center in the field of organic chemistry. Fluorine is very important in the science of organofluoride. Indicates other important properties, such as high-density recycling such as fluorine gas (F<sub>2</sub>), low nucleophilicity such as fluoride and generally low availability of "F+" sources (select fluor type F + essential), among others. Light reagents are widely used in salt-based metal conversion which is used to prepare important fuel-efficient purposes. The process finds the use of fluorine chemical compounds containing agrochemicals and pharmaceutical drugs.

**Non-invasive Physiology and Pharmacology**

Using <sup>19</sup>F Magnetic Resonance Magnetic resonance imaging (MRI) is very important in the detection of various diseases in the field of radiology. <sup>19</sup>F has become important in MRI and in spectroscopic (NMR) investigations. <sup>19</sup>F does not send any background signal in the body but it has high NMR sensitivity. There are numerous reports available on the syntheses of molecules which employ the sensitivity of F atom to its microenvironment; it also involves other important aspects such as volume, vascular flow, hypoxia reporters, gene reporter molecules, metal ion concentrations. The fluorine atom provides an exciting tool for diverse spectroscopic and imaging applications using Magnetic Resonance. The organic chemistry of fluorine is widely established and it can provide a stable moiety for interrogating many aspects of physiology and pharmacology in vivo. Strong NMR signal, minimal background signal and exquisite sensitivity to changes in the microenvironment have been exploited to design and apply diverse reporter molecules. Classes of agents are presented to investigate gene activity, pH, metal ion concentrations

(e.g., Ca<sup>2+</sup>, Mg<sup>2+</sup>, Na<sup>+</sup>), oxygen tension, hypoxia, vascular flow and vascular volume.

**Fluorine Containing Toxoids as Anticancer Operators**  
Paclitaxel (Taxol) and docetaxel (a "toxoid") are two of the most broadly utilized chemotherapeutic specialists. Another toxoid cabazitaxel was affirmed by FDA for hormone-hard-headed prostate malignancy after mixing with prednisone. Currently, various novel toxoids are in different phases of clinical and preclinical advancement. In spite of ongoing advances in symptomatic and remedial modalities (otherwise known as theranostics modalities), malignancy remains a noteworthy wellspring of misery and mortality all over the world. The nearness of fluorine among pharmaceuticals (including radiopharmaceuticals, F-drugs) has greatly affected a number of essential restorative applications (such as treatment and imaging). malignant tissues and its utilization in clinical administration. In breast malignant growth, entire body (WB) PET / CT is utilized for useful imaging since it is valuable for arranging lymph hubs and inaccessible metastasis.

#### BETTER DRUG METABOLIC STABILITY

Cytochrome P450 (liver enzyme) is responsible for the oxidation of lipophilic compounds which are easily oxidized by liver enzymes. So, due to low drug metabolic stability, a big challenge is posed in drug discovery. This problem may be resolved if a fluorine atom is introduced into the compound or by enhancing the polarity of that compound for the purpose of altering the route, rate, or level of drug metabolism. It can be done by substituting fluorine at a metabolically labile site. Fluorine substitution at the adjacent position results in either the decrease or increase of biotransformation which depends upon the following,

1. Whether the metabolic attachment is nucleophilic or electrophilic
2. Whether resonance or inductive effect of the inductive effect of fluorine may be produced in a saturated.

#### ANTICANCER FLUORINATED DRUGS

An initially marketed drug for cancer treatment is 5-fluorouracil (5FU) which is an antimetabolite. This drug enters into the cells through the uracil transporter and undergoes biotransformation into a variety of

metabolites including fluorodeoxyuridine monophosphate. Due to the high redox potential and small size of fluorine, this metabolite reacts with co-substrates 5,10-methylene tetrahydrofolate and thymidylate synthase (an enzyme) to produce a stable ternary complex, thus preventing the methylation of deoxy uridine monophosphate (native substrate). As a result, the synthesis of deoxythymidine monophosphate is stopped. Cancer cells which increase in number rapidly as compared to healthy normal cells are excessively affected by the drug. A cardiotoxic drug such as 5FU is responsible for the metabolism of drug to lethal metabolite.

The utilization of drugs targeted towards the central nervous system (CNS) has been very useful in the case of many peripherally acting drugs. Fluorine containing CNS drugs such as sevoflurane, triflupromazine, and fluconazole are most important in this regard.

#### FLUORINE CONTAINING ANAESTHETICS

Fluorine containing compounds such as desflurane, enflurane, sevoflurane, isoflurane and halothane were investigated and it was found that they are bio-transformed into toxic metabolites, which is the reason of the toxicity of these medicines. Human liver is responsible for the metabolism of fluorine anaesthetics into inorganic fluoride and hexa-fluoro-isopropanol. At saturating substrate concentrations, the order of anaesthetic metabolism (as shown by the production of fluoride) was methoxyflurane >sevoflurane >enflurane>isoflurane>desflurane>0. Till now, inorganic fluoride has been considered as the main etiological specie for fluorinated anaesthetic nephrotoxicity.

#### STEROIDAL INFLAMMATORY AND PROTON PUMP INHIBITOR FLUORINATED DRUGS

Fluticasone propionate is an anti-inflammatory agent of steroidal origin; it is used for the treatment of inflammation associated with psoriasis and dermatoses. In combination with salmeterol, it is used for the treatment of asthma. Lansoprazole is the most successful commercial drug regulating the gastric acid secretion. Other important drugs such as omeprazole, pantoprazole, rabeprazole and pantoprazole contain difluoromethoxyl moiety. They are advised to treat esophageal inflammation, peptic ulcers and heartburn.

For the substitution of protons (H<sup>+</sup>) by potassium ions (K<sup>+</sup>) in stomach lumen, lansoprazole acts as an important 'proton pump inhibitor' (PPI); it involves a metabolic process which is driven by adenosine triphosphate.

#### CONCLUSION

In medicine, fluorine has various applications such as it is used in the development of various drugs and drug discovery. It is used to cure cancer and also for its detection. Labelled <sup>18</sup>F is widely used for cancer treatment and for its diagnosis. <sup>18</sup>F plays a vital role in diagnosing tumors. In the major technique of PET imaging, fluorine-18 and also fluorine-19 act as radiolabel tracer atoms. As fluorine has various applications in the medical field, so it may be used in drug discovery and also for its development. Hence, it is concluded that fluorine and its derivatives play a vital role in human life and are used to cure and detect different types of diseases.

#### REFERENCES

- [1] Kirk KL, Yoshida S, Haufe G. Synthesis and biochemical evaluation of fluorinated monoamine oxidase inhibitors. In: Tressaud A, Haufe G, eds. Fluorine and Health: Molecular Imaging, Biomedical Materials and Pharmaceuticals. London: Elsevier;2008.661-667
- [2] Gillis EP, Eastman KJ, Hill MD, Donnelly DJ Meanwell NA. Applications of fluorine in medicinal chemistry. J Med Chem. 2015;58(21): 8315–8359.
- [3] Swallow S. Fluorine in medicinal chemistry. In: Lawton G, Witty D, eds. Progress in Medicinal Chemistry. London: Elsevier; 2015. 65–133.
- [4] Isanbor C, O'Hagan D. Fluorine in medicinal chemistry: a review of anti-cancer agents. J Fluorine Chem. 2006;127(3): 303–319.
- [5] Arntson KE, Pomerantz WC. Protein-observed fluorine NMR: a bioorthogonal approach for small molecule discovery: miniperspective. J Med Chem. 2015;59(11): 5158–5171.
- [6] O'Hagan D, Harper DB. Fluorine-containing natural products. J Fluorine Chem. 1999;100(1-2): 127–133.
- [7] Shah P, West well AD. The role of fluorine in medicinal chemistry. J Enzyme Inhib Med Chem. 2007;22(5): 527–540.

- [8] Ojima I. Use of fluorine in the medicinal chemistry and chemical biology of bioactive compounds—a case study on fluorinated taxane anticancer agents. *Chem Bio Chem*. 2004;5(5): 628–635.
- [9] Ghorab MM, Alsaid MS, El-Gaby MS, Elaasser MM, Nissan YM. Antimicrobial and anticancer activity of some novel fluorinated thiourea derivatives carrying sulfonamide moieties: synthesis, biological evaluation and molecular docking. *Chem Central J*. 2017;11(1): 32.
- [10] Hussain S, Bukhari IH, Ali S, Shahzadi S, Shahid M, Munawar KS. Synthesis and spectroscopic and thermogravimetric characterization of heterobimetallic complexes with Sn (IV) and Pd (II); DNA binding, alkaline phosphatase inhibition and biological activity studies. *J Coord Chem*. 2015;68(4): 662–677.
- [11] Hussain S, Ali S, Shahzadi S, Tahir MN, Shahid M. Synthesis, characterization, biological activities, crystal structure and DNA binding of organotin (IV) 5-chlorosalicylates. *J Coord Chem*. 2015;68(14): 2369–2387.
- [12] Mariam S, Hussain S, Ali S, Shahzadi S, Ramzan S, Shahid M. Homobimetallic (Sn, Sn) Complexes with [2-Dithiocarboxy (methyl) amino] acetic acid: synthesis, characterization and biological studies. *Iran J Sci Technol, Trans A: Sci*. 2018;42(3): 1277–1284.
- [13] Saleem S, Nazli Z-e-h, Saleem N, Bashir MS, Hussain S. Synthesis, spectroscopy and biological studies of chalcone derived pyrimidines. *Der Pharma Chemica*. 2018;10(10): 110–117.
- [14] Dinoiu V. Fluorine chemistry: past, present and future. *Rev Roum Chim*. 2006;51(12): 1141.
- [15] Chua M-S, Shi D-F, Wrigley S, Bradshaw TD, Hutchinson I Stevens MF. Antitumor benzothiazoles. 7. Synthesis of 2-(4-acylamino-phenyl) benzothiazoles and investigations into the role of acetylation in the antitumor activities of the parent amines. *J Med Chem*. 1999;42(3): 381–392.