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Deuteration as a Tool for Enhancing the Half-Life of Drug

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Abstract: ***The aim of the article is that deuteration of any compounds leads to the enhancement of metabolic activity.The substitution of Carbon-Hydrogen bond by Carbon –Deutrieum help for enhancing pharmacokinetic profile of the drug. Since C-D bond is ten time more tough to C-H bond .Nowadays, many drug molecules are deuterated to increase the residence time of the drug as well as diminution the metabolism of the drug.Deuterated drugs also finds various therapeutic applications.The deuterated drugs is also approved by Food and Drug Administration. The deuteration helps in increasing the dwell time of the drug and reducing frequency of dosing.***

Keywords: ***Deuteration, half- life, pharmacokinetics, therapeutic effects***

I. INTRODUCTION

Drug research and development is a more difficult process because of increased cost and risk associated with the process.(1)Deuterium is a isotope of water , containing0.015%deuteriumoxide. In nuclear reactors it is basically used as moderators.(2)When living systems are exposed to D_2O the two affects are basically arises.One is due to effect of D_2O itself and the second affect is due to capability to substitute hydrogen withdeuterium in body. The carbon -deuteriumbond resistant to enzymatic cleavage as compared to C-H bond. The compounds containing C-D bonds are more stable than compounds containing C-H bond.(3) D_2O also has numerous therapeutic applications and it is used as therapeutic agent against pancreatic cancer, stability of cells and tissues, stability of macromolecules and helps in determination of total body water.(4) Recently,a number of patents are granted or filed regarding the potential therapeutic applications of D_2O.(5)

II. THERAPEUTIC APPLICATION OF DEUTERATED COMPOUNDS

The deuteratedrug can be used in the treatment of various human diseases.Edward M. Russak et al (2018) studied that first deuterated drugisDeutetrabenazine which is deutrated form of tetrabenazine. Deutetrabenazine is the drug which is accepted by Food and Drug Administration (FDA)and the drug is used in the treatment of Huntington's disease and tardive dyskinesia. (6)

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The deutrated drug is also responsible for improved metabolism of drug.The another study which was done by Graham S Timmins et al (2014) who studied that **t**ransformation of drugs into deuterated formhas better pharmacokinetic or toxicological properties. This is because due to the presence stronger deuterium-carbon bond which is responsible for their improved metabolism.The ability of deutriuem oxide for treatment of various diseases ,use of deuteriuem oxide in experiments ,artificial synthesis of deuterium-labeled compounds was studied by Wendell Costa Bila (2017).(7)

Deuterated Efavirenz finds use for nephrotoxicity. Scott L. Harbeson et al (2014) studied thatthe deuteratedefavirenzuse to clarify the nephrotoxicity in mice. Efavirenz is ainhibitor of reverse transcriptase which is used for treatment of HIV. The substitution of hydrogenof cyclopropylmethineby means of deuterium, thus dropping the metabolism and reduces the severity of nephrotoxicity.(8)

The secondary amines can be useful in synthesis of larger polymers and organic molecules.The study onoptoelectronic devices was doneby Anwen M. Krause-Heuer 2014. The production of organic molecules or polymers can be done by usingdeuterated arylamines(9).A study was done byRobert B. Raffaet al (2018)in which he studied that the(C-H) bond has less stability in comparison to C-D bond. It was found that if deuterium is located suitably in drug so the carbon deutriuem bond does not undergo metabolic breakdown which leads to enhance the stability of the drug(10).

Similarly, a study was done by Sarah Cargnin (2019) which revealed that there are many deutrated drugs in clinincal development stage. About 20 drugs are under this stage in which 6 drugs reaches the IIIphase clinical trials.Through out previous years more focus is given to the deuterated drugs and in 2018, novel drug, HC-1119, enter in clinical development of deuterated drug.(11).

Another important study was done by Sukhninder Kaur*et al* (2017) where it was emphasize that deuteration take part in enhancing half life of drug. The bond formation between carbon hydrogen is weak as compared to carbon with deuterium.This ultimately leads to increase in the biological half-life of the drug (12). Cuibo Liu (2018) researched the halides deuteration using heavy water. The deuteration strategy show improved results and tolerances. The deuterated acids and alkynes are useful in various reactions like suzuki coupling and click reaction, for production of multifaceted deuterated compound (13).

Raman Sharma et al (2012) studied that the pharmacokinetic profile of drugscan be altered by means of deuterium.

It was found that the *ex- vivo*and *in-vivo* methods suggested that the deuterated carbazeran and zoniporidehave decreased metabolism and it helps in increasing the half life of the drugs.MałgorzataCebo(2014)*et al* investigated that the exchange in D-H in imidazole gets affected by phosphorylation of histidine side chain in peptides. The consequencesreveal that phosphorylation considerablyslow the speed of the DHX reaction. (14)

Maicon Guerra de Miranda develop deuterated compound which is frequently used as biomarkers in petroleum and related sample.(15)The benzopyran deuterated was prepared by Yanmei Zhang, Micky D. Tortorella *et al* (2014).It is used as novelinhibitor of COX-2.The compound has better pharmacokinetic profile than the previous one. The novel compound showeffective role in various inflmmatory and painful conditions.(16)In 2016 Jinfang Jiang *et al* studied that the Enzalutamide (ENT) which is responsible for inhibition of the androgen receptor was accepted formanagement of prostate cancer by USFDA.In this the *N*–CH_3 moiety were substituted by deuterium. This shows that the drug has good pharmacokinetic profile. (17)

III. CONCLUSION

The article concluded that the deuteration is a vitalfactor in enhancing half-life of the drug.The deuterated drugs takes more time to get cleared from the systemic circulation.It helps to increase the residential of drug inside the body and thus helpful in reducing the dosing regimen which can ultimately leads to enhance the dosage regimen.

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