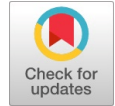


# Deuteration as a Tool for Enhancing the Half-Life of Drug



Vijay Kumar, Archana Dhyani, N Singh

**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-Deuterium 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, containing 0.015% deuterium oxide. In nuclear reactors it is basically used as moderators. (2) When living systems are exposed to D<sub>2</sub>O the two affects are basically arises. One is due to effect of D<sub>2</sub>O itself and the second affect is due to capability to substitute hydrogen with deuterium in body. The carbon-deuterium bond 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<sub>2</sub>O 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<sub>2</sub>O. (5)

## II. THERAPEUTIC APPLICATION OF DEUTERATED COMPOUNDS

The deuterated drug can be used in the treatment of various human diseases. Edward M. Russak et al (2018) studied that first deuterated drug is Deutetrabenazine which is deuterated 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 deuterated 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 transformation of drugs into deuterated form has 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 deuterium oxide for treatment of various diseases, use of deuterium 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 that the deuterated efavirenz use to clarify the nephrotoxicity in mice. Efavirenz is an inhibitor of reverse transcriptase which is used for treatment of HIV. The substitution of hydrogen of cyclopropylmethine by 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 on optoelectronic devices was done by Anwen M. Krause-Heuer 2014. The production of organic molecules or polymers can be done by using deuterated arylamines (9). A study was done by Robert B. Raffa et 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 deuterium 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 deuterated drugs in clinical development stage. About 20 drugs are under this stage in which 6 drugs reaches the III phase 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 Sukhinder Kaure 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 drug can be altered by means of deuterium.



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

Maicon Guerra de Miranda developed 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 novel inhibitor of COX-2. The compound has better pharmacokinetic profile than the previous one. The novel compound shows effective role in various inflammatory 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 for management of prostate cancer by USFDA. In this the *N*-CH<sub>3</sub> 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 vital factor in enhancing half-life of the drug. The deuterated drug takes more time to get cleared from the systemic circulation. It helps to increase the residence time of drug inside the body and thus helpful in reducing the dosing regimen which can ultimately lead to enhance the dosage regimen.

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