REVIEW ARTICLE

# A Comprehensive Review of Deflazacort with Special Reference to Pharmacological Profile and Pharmaceutical Validation Processes

Swati Pund[1*], Vaibhav Changediya[2], Vikas Rajurkar[3]

[1]*Department of Quality Assurance, Dr. Vedprakash Patil Pharmacy College, Chhatrapati Sambhajinagar, Dr. Babasaheb Ambedkar Technological University, Lonere, Maharashtra, India.*
[2]*Department of Pharmaceutics, Dr. Vedprakash Patil Pharmacy College, Chhatrapati Sambhajinagar, Dr. Babasaheb Ambedkar Technological University, Lonere, Maharashtra, India.*
[3]*Department of Pharmaceutical Chemistry, Dr. Vedprakash Patil Pharmacy College, Chhatrapati Sambhajinagar, Dr. Babasaheb Ambedkar Technological University, Lonere, Maharashtra, India.*

***Received: 08th March, 2023; Revised: 21st April, 2023; Accepted: 14th June, 2023; Available Online: 25th June, 2023***

**ABSTRACT**

Deflazacort is a prednisolone-derived immunosuppressant and anti-inflammatory. It controls cytokines and immune cell development. It may increase muscle cell proliferation and reduce muscle breakdown to enhance Duchenne muscular dystrophy muscle strength and function. Pharmaceutical companies aim to produce high-quality drugs at low prices. Pharmaceutical formulation discovery, development, and evaluation require validated methods. Validation ensures quality and reliability throughout the manufacturing process. The validation procedure evaluates accuracy, specificity, precision, and system applicability to guarantee the analytical technique used to analyze medicine-related samples is reliable. This paper describes the deflazacort technique development and validation. Google Scholar, Pub-Med, and Shodganga are utilized to gather information.

**Keywords:** Deflazacort, ADME, Method development, Validation.

International Journal of Drug Delivery Technology (2023); DOI: 10.25258/ijddt.13.2.43

**How to cite this article:** Pund S, Changediya V, Rajurkar V. A Comprehensive Review of Deflazacort with Special Reference to Pharmacological Profile and Pharmaceutical Validation Processes. International Journal of Drug Delivery Technology. 2023;13(2):749-752.

**Source of support:** Nil.

**Conflict of interest:** None

## INTRODUCTION

Deflazacort, an oxazoline derivative of prednisolone.[1] The glucocorticoid prodrug deflazacort is metabolized into an active form known as 21-desacetyldeflazacort. Deflazacort inhibits the growth of $CD4^+$ lymphocytes in the culture, which results in decreased cytokine output. The decline in $CD4^+$ cells and subsequent increase in $CD8^+$ cells has anti-inflammatory and immunosuppressive effects.[2] Although the exact method through which deflazacort improves muscle potency and utility in individuals with duchenne muscular dystrophy remains unknown, it is believed to entail increased muscle cell proliferation with decreased muscle breakdown, leading to an increase in total muscle mass. Dystrophin protein and other proteins in a positive feedback loop with it may be influenced by deflazacort's ability to modulate transcription.[3]

### Pharmacokinetics

*Absorption*

Deflazacort is well-absorbed orally after administration. The absolute bioavailability of deflazacort is approximately 70 to 90%. Food intake does not significantly affect the absorption of deflazacort.

*Distribution*

Deflazacort has a moderate volume of distribution. It binds extensively to plasma proteins, primarily albumin and transcortin (corticosteroid-binding globulin). The binding to proteins influences its distribution and reduces the concentration of free, active drug.

*Metabolism*

Deflazacort undergoes extensive metabolism in the liver. It is primarily metabolized by cytochrome P450 enzyme, mainly CYP3A4. Major metabolite formed 21-desacetyldeflazacort that is pharmacologically active but has reduced glucocorticoid potency compared to deflazacort.

*Excretion*

Deflazacort and its metabolites are excreted in urine and feces. The elimination half-life of deflazacort is approximately 1.5 to 2 hours, while the half-life of the active metabolite, 21-desacetyldeflazacort, is longer at around 18 to 36 hours.

**Author for Correspondence: pundswati05@gmail.com*

**Special Populations**

*Elderly*

The pharmacokinetics of deflazacort in the elderly have not been extensively studied. However, age-related changes in liver and kidney function may affect the drug's metabolism and elimination.

*Pediatrics*

Deflazacort has been studied and approved for use in children with certain medical conditions. The pharmacokinetics in pediatric patients may vary, and dosing should be adjusted accordingly.

*Drug interactions*

Deflazacort can interact with drugs that induce or inhibit the cytochrome P450 enzyme system, particularly CYP3A4. Deflazacort levels may be increased when co-administered with potent CYP3A4 inhibitors like ketoconazole or erythromycin and may be decreased when co-administered with CYP3A4 inducers like rifampicin or phenytoin. Care should be taken when combining deflazacort with other medications to avoid potential interactions.

It's important to note that the information provided here is a general overview and may not encompass all possible aspects of deflazacort's pharmacokinetics. It's always advisable to consult the prescribing physician or refer to the drug's package insert for more detailed and specific information.[4]

The primary goal of the pharmaceutical industry is the consistent, high-quality production of essential characteristics and qualities at reasonable costs.

The discovery, development, and assessment of pharmaceutical formulation medications require the establishment of a methodology. The primary objective of this evaluation was to examine the process used for the medication's formulation, development, and validation, to the entire production run of the product. The results of an analytical technique used to assess the quality of medicine-related samples must be trusted if they are to be used in clinical practise. Good manufacturing practise (GMP) standards require the pharmaceutical business to have a documented validation policy outlining the steps for doing validation, the different types of validation, and the validation policy itself. The efficient operation of pharmaceutical companies relies heavily on validation. The raw materials, intermediate steps, and final product were all validated for stability. Accuracy, specificity, precision, LoD, LoQ, ruggedness, robustness, and system applicability testing using an example of a few medicines show that the technique was established correctly and that the validation parameters are described. The regular and stability tests employ all of the validation parameters.[5] Here we summarize some method development and validation of deflazacort.

1. This work developed and validated an RP-HPLC dissolution quality control of 6 mg tablets deflazacort, medication utilized to prevent organ transplantation rejection. DEF decomposed as a function of the dissolving media and sink conditions at 37°C. However, DEF dissolution was unaffected by a breakdown in water. Paddle, 50 rpm, 500 mL water, and 37°C were found to be optimal for dissolution testing. Different in vitro release profiles were observed between the 6 mg DEF tablets created by two laboratories, which collectively represented every brands available in national market. Both formulations showed a similar relationship between disintegration and *in-vitro* dissolution. The dissolve test for quality control of 6 mg DEF pills was adequate.[6]
2. A simple, specific, precise, and exact first-order derivative spectrophotometric approach was devised and validated for the simultaneous purpose of deflazacort and tamsulosin hydrochloride in tablet form. The wavelengths of deflazacort (266 nm) and tamsulosin hydrochloride (242 nm) were calculated. Deflazacort's linearity range was 8–40 µg/mL and tamsulosin hydrochloride's 1.6–8. Deflazacort and tamsulosin hydrochloride had 0.9916 and 0.9971 correlation coefficients. Deflazacort recovered 99.95–100.42% and tamsulosin hydrochloride 99.31–100.31.[7]
3. Deflazacort was detected quantitatively in tablets and compounded capsules using a validated method developed utilizing RH-HPLC chromatography was performed on a C18 column using 80:20 (v/v) acetonitrile with water. The flow rate was 1-mL/min. The cutoff for ultraviolet (UV) detection was set at 240 nm. The approach was found to be linear, precise (RSD< 2%) both within as well as between days, and accurate (recovery >98%). The specificity and reliability of the approach were also verified. The outcomes verified that the recommended approach works as planned.[8]
4. Anti-inflammatory and immunosuppressive glucocorticoid deflazacort. No pharmacopeia recognizes this medicine. Method A uses a basic absorptive value to measure deflazacort in ethanol with water at 247 nm. Approach B is a derivative spectrophotometric approach that measures deflazacort at 276.5 and 228.2 nm using zero & first-order derivatives.[9]
5. Method C of AUC analysis. The total absorbance at both 230.2 and 264.4 nm is computed using this method. The technique D HPLC setup consisted of a C18 column, mobile phase of acetonitrile: methanol: phosphate buffer pH 7.0, 90:5:5 (v/v/v) 1-mL/min flow rate, and 247 nm detection. The retention time for the peak was 4.025 minutes. Standard deviation (0.5929868), asymmetry (1.1732), and column efficiency (718610.6) all point to a significant improvement in eluting performance as compared to the previous HPLC method. The new approach has a somewhat lower detection limit. Since no pharmacopeia routinely analyses deflazacort, the innovative RP-HPLC and spectroscopic procedures valuable for drug manufacturers and quality control.[10]
6. The RP-HPLC method by UV detection is used to assess deflazacort in raw materials, human blood samples, pharmaceuticals, and *in-vitro* drug dissolution

investigations because it is easy, sensitive, reproducible, and validated. The molecules were separated using a $C_{18}$ column with mobile phase of(27:20:53, v/v/v) acetonitrile, methanol, and 0.067 M KH2PO4 at a pH of 6.5, adding 3M NaOH. The analyses were solid and statistically sound. Limits of detection and quantification were 2.05 and 6.83 ng $mL^{-1}$ in the mobile phase, and 4.06 and 13.55 ng/$mL^{-1}$ in human serum samples. The method gave a linear response between 25 and 30,000 ng $mL^{-1}$ in blood samples and 10–30,000 ng $mL^{-1}$ in mobile phase. Assay precision in mobile phase was 0.92% intra- and inter-day, while 1.48% in human serum samples using this method. The drug's tablet form, the concentration of human serum, and the results of drug-dissolving studies were all determined by this method. Findings were reliable, repeatable, and devoid of excipients.[10]

7. This study describes sensitive and reproducible methods for quantifying deflazacort in its breakdown product. Using acquity UPLC BEH C18 columns with acetonitrile & water (40:60 V/V) at 0.2 mL/minute in UPLC, we separated the medicine from its breakdown product using high-performance liquid chromatography (HPLC). UV light measured at 240.1 nm. Oxidation, acid, base, hydrolysis, heat, and photolysis degraded deflazacort. The medication survived aqueous, heat, and neutral stress. Deflazacort decomposed under alkaline, acid, and photolytic stress in forced-degradation studies. Present work additionally emphasizes degradant separation, characterization, and identification. Thus, deflazacort degradants were sought. NMR, FTIR, and LC-MS found a deflazacort breakdown product.[11]
8. Two eco-friendly chromatographic separation methods were devised to simultaneously test tamsulosin HCl plus deflazacort in their binary combination. Both procedures used green mobile phase with ethanol and dilute acetic acid. First, RP-HPLC with photodiode array detection quantified together medications at wavelengths of 225 and 245 nm; with linearity range of 0.20–100 and 0.50–200 μg/$mL^{-1}$, respectively. The second approach employed HPTLC with densitometry at 225 nm to separate and identify tamsulosin HCl and Deflazacort at 0.30–4.0 and 0.70–5.0 μg $band^{-1}$, respectively. ICH-compliant procedures were validated. Since deflazacort has a strong propensity for degradation to its active metabolite, 21-hydroxy deflazacort, the proposed methods were examined for their capacity to identify the two drugs in the presence of deflazacort and rated based on the chromatographic system appropriateness criteria. As suggested in the methodology section, tamsulosin HCl and deflazacort tablets were analysed for their active ingredients using RP-HPLC to track their *in-vitro* dissolution profiles. Analytical eco-scale was used to compare suggested procedures to official or reported drug determination methodologies.[12]
9. A simultaneous estimation of deflazacort and tamsulosin hydrochloride combined dose form was developed and validated using RP-HPLC. Deflazacort and tamsulosin hydrochloride both have 1.000 co-relation coefficients and linearity ranges of 180–420 and 2.4–5.6 g/mL, respectively, when measured by RP-HPLC. Tamsulosin hydrochloride recovered 99.78% and deflazacort 99.89%. Tamsulosin hydrochloride's LoD was 0.04 g/mL, while deflazacort's was 2.34 g/mL. The LoQs for deflazacort with tamsulosin hydrochloride were 7.11 and 0.13 g/mL, respectively. For deflazacort and tamsulosin hydrochloride, the label conformance was 100.14 and 100.27%.[13]
10. A selective RP-HPLC/PAD approach can simultaneously measure deflazacort, aprepitant, and granisetron, three chemotherapeutic medications. The three medicines were chromatographed on a C18 column using acetonitrile: triethylamine (80:20 v/v, with isocratic elution and photodiode array monitoring at 220 nm. The validated approach follows ICH recommendations.[14]
11. It was estimated in bulk medication and in-house nanosponges formulation using a simple, quick, and selective RP-HPLC method. Deflazacort, an oxazoline derivative of prednisolone, has significant tissue glucocorticoid receptor binding affinity and anti-inflammatory and immunosuppressive properties. Deflazacort dramatically reduces mononuclear cell growth and cytokine release from human peripheral blood. At a flow rate of 1.0 mL/min, 20 mM KH2PO4: Acetonitrile (20:80v/v, pH 4.0 with OPA) was used as the mobile phase for separation on a Thermo C18 analytical column (250 mm 4.6 mm i.d., 5.0 μm). UV light at 242 nm is measured by sensors. After 15 minutes of chromatographic analysis, DFZC was eluted at a time of 4.085 ± 0.002 minutes. All of the correctnesses, exactnesses, specificities, linearities, and sensitivities were checked and approved. The HPLC method was shown to be straightforward, sensitive, rapid, dependable, and repeatable through validation. DFZC in pharmaceutical formulation could be measured with the developed and verified method. The proposed approach can determine DFZC (In-house) nanosponges formulation due to its high recovery and low relative standard deviation.[15]
12. Anti-inflammatory and immunosuppressive deflazacort is a prednisolone methyl-oxazoline derivative. The prodrug quickly becomes 21-desacetyl deflazacort. Using liquid chromatography-tandem mass spectrometry human plasma 21-desacetyl deflazacort was measured. Solid-phase extraction removed 21-desacetyl deflazacort and internal standard. Reversed phase column and positive mode ESI tandem mass spectrometry evaluated the samples. Assay was linear from 0.5 to 100 μg/mL using 250 μL samples. LLoQ was 0.5. Specificity, linearity, precision, accuracy, and stability were validated.[16]
13. A reverse phase HPLC method for pharmaceutical dosage form deflazacort assessment is simple, specific, fast, and efficient. As a means of separation, a Hypersil BDS C18 column was put to use. Buffer solution for the mobile phase contained ammonium acetate and acetonitrile (1:1 v/v).

1-mL/min flow rate, 254 nm wavelength. Deflazacort had a retention time of 6.03 minutes. The concentration range examined was 20–100 µg/mL, where a linear relationship was found with a correlation coefficient of 0.998. The proposed strategy has been statistically evaluated, and recovery experiments have shown its accuracy. An accurate, exact, linear, robust, easy, quick, and selective RP-HPLC technique has been presented for measurement of deflazacort dosage form.[17]

## CONCLUSION

Deflazacort inhibits growth of CD4+ lymphocytes and modulates cytokine output, leading to a decrease in inflammation. It is well-absorbed orally, extensively bound to plasma proteins, metabolized in the liver primarily by the CYP3A4 enzyme, and excreted in urine and feces. Its pharmacokinetics may vary in special populations such as the elderly and pediatric patients. Care should be taken when co-administering deflazacort with drugs that affect the cytochrome P450 enzyme system. Deflazacort analysis has been validated using several methods, including RP-HPLC, spectrophotometric, and derivative spectrophotometric techniques. These methods demonstrate accuracy, precision, and specificity in quantifying deflazacort in various formulations and samples. Overall, deflazacort holds promise as a therapeutic option for various conditions, and its formulation and analysis methods have been well-established and validated to ensure quality control in its production.

## REFERENCES


1. Bylo M, Farewell R, Coppenrath VA, Yogaratnam D. A review of deflazacort for patients with Duchenne muscular dystrophy. Annals of Pharmacotherapy. 2020 Aug;54(8):788-94.
2. Markham A, Bryson HM. Deflazacort: A review of its pharmacological properties and therapeutic efficacy. Drugs. 1995 Aug;50:317-33.
3. Angelini C, Peterle E. Old and new therapeutic developments in steroid treatment in Duchenne muscular dystrophy. Acta myologica. 2012 May;31(1):9.
4. Möllmann H, Hochhaus G, Rohatagi S, Barth J, Derendorf H. Pharmacokinetic/pharmacodynamic evaluation of deflazacort in comparison to methylprednisolone and prednisolone. Pharmaceutical research. 1995 Jul;12:1096-100.
5. Sharma S, Goyal S, Chauhan K. A review on analytical method development and validation. International Journal of Applied Pharmaceutics. 2018 Nov 7;10(6):8-15.
6. Sperandeo NR, Kassuha DE. Development and validation of a dissolution test for 6 mg deflazacort tablets. Scientia Pharmaceutica. 2009 Sep;77(3):679-94.
7. Rupapara VV, Dedania ZR, Dedania R. UV-spectroscopy method development and validation of deflazacort and tamsulosin hydrochloride in combined dosage form. World Journal of Pharmaceutical Research. 2018 Jun 5;7(15):538-49.
8. Corrêa GM, Bellé LP, Bajerski L, Borgmann SH, Cardoso SG. Development and validation of a reversed-phase HPLC method for the determination of deflazacort in pharmaceutical dosage forms. Chromatographia. 2007 May;65:591-4.
9. Puranik M, Shambharkar S, Nimbalkar S, Mahapatra DK. Comparison of UV-spectrophotometric and RP-HPLC methods for estimation of deflazacort in solid dosage form. Journal of Applied Pharmaceutical Science. 2020 Jul 4;10(7):082-8.
10. Özkan Y, Savaşer A, Taş Ç, Uslu B, Özkan SA. Drug dissolution studies and determination of deflazacort in pharmaceutical formulations and human serum samples by RP-HPLC. Journal of liquid chromatography & related technologies. 2003 Aug 1;26(13):2141-56.
11. Deshmukh R, Sharma L, Tekade M, Kesharwani P, Trivedi P, Tekade RK. Force degradation behavior of glucocorticoid deflazacort by UPLC: isolation, identification and characterization of degradant by FTIR, NMR and mass analysis. Journal of biomedical research. 2016 Mar;30(2):149.
12. Boltia SA, Abdelkawy M, Mohamed TA, Mostafa NN. Eco-friendly RP-HPLC and HPTLC methods for simultaneous determination of tamsulosin hydrochloride and deflazacort in the presence of 21-hydroxy deflazacort and testing the in-vitro dissolution of the combined dosage form via RP-HPLC method. Chromatographia. 2021 Mar;84(3):285-95.
13. Sidram KL, Mubarak TA. RP-HPLC Method Development and Validation for Simultaneous Determination of Deflazacort and Tamsulosin Hydrochloride. International Journal of Pharmaceutical Research (09752366). 2021 Jul 1;13(3).
14. Tantawy MA, Alweshahy S, Elshabasy DA, Youssef NF. Simultaneous determination of co-administrated deflazacort, aprepitant and granisetron in dosage forms and spiked human plasma by RP-HPLC/PAD. Journal of Chromatographic Science. 2019 Nov;57(9):790-8.
15. Mishra S, Sharma N, Jain S. HPLC method development and validation for the estimation of deflazacort in nanosponges formulations. International Journal of Pharmaceutical Research (09752366). 2020 Oct 1;12(4).
16. Karthikeyan S. A LC-MS/MS method for the quantification of deflazacort metabolite in human plasma: development, validation and application to a pharmacokinetic study. Journal of Drug Delivery and Therapeutics. 2013 Mar 15;3(2).
17. Chougule DD, Naikwade NS. Development and validation of high performance liquid chromatographic method for estimation of deflazacort in pharmaceutical formulation. Asian Journal of research in chemistry. 2011;4(1):140-2.