IJBPAS, December, 2023, 12(12): 5751-5755

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

A REVIEW ON ANALYTICAL METHOD DEVELOPMENT AND VALIDATION FOR DETERMINATION OF ALFACALCIDOL IN BULK AND TABLET DOSAGE FORM

ARUN P[1], VIJEY AANANDHI M[2] AND SHANMUGAM SUNDHRAM P[3*]

Department of Pharmaceutical Chemistry and Analysis, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS) Pallavaram, Chennai, TamilNadu, India, Pincode - 600117

***Corresponding Author: Dr. Shanmugam Sundaram P: E Mail: director.sps@velsuniv.ac.in**

Received 19th Oct. 2022; Revised 16th Nov. 2022; Accepted 8th April 2023; Available online 1st Dec. 2023

https://doi.org/10.31032/IJBPAS/2023/12.12.7645

ABSTRACT

HPLC is an analytical method and key tool for the drug separation, drug quality, monitoring of drugs and in the research of life science. The analysis and separation of non-volatile compounds are majorly done by HPLC method. HPLC deals with variety of applications like high sensitivity, accuracy, precision and resolution. The retention time in the RP-HPLC is calculated fewer than 100% in the aqueous condition. The aim of the work was to develop RP-HPLC method for combination of drug and it is validated as per ICH guidelines My whole work is to discuss the analytical method development, validation and optimization of alfacalcidol by RP-HPLC developed for the determination of osteoporosis and it stimulates intestinal calcium absorption with the selection of mobile phase, review of literature, selection of chromatographic conditions, wavelength and detectors used for the quantification of combination of drug which will be useful for the research scholars for development and optimization of drug combination

Keywords: Method development, validation, RP-HPLC, application, quantification

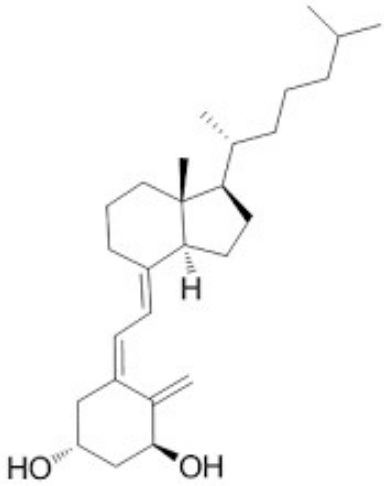
INTRODUCTION

A synthetic vitamin D analogue called alfacalcidol (1-hydroxyvitamin D3) was first used in medicine in the early 1970s.One of the most potent and quickly acting

substances now employed in the prevention and treatment of vitamin D deficiency disorders and hypocalcemia is calcitriol (1,25-dihydroxyvitamin D3), which it is a prodrug. The capacity to stimulate calcium and phosphorus absorption, reverse myopathy, promote bone mineralization, and reabsorb completely mineralized bone are all therapeutic benefits of alfacalcidol. Ergocalciferol and calcitriol are commercial vitamin D compounds that are similar. Establishing an appropriate analytical technique for a certain active component in a more focused, accurate, and exact manner will help to enhance the condition and parameter that should be adhered to in the development and validation **[1]**.

Due to its prolonged half-life, alfacalcidol has been utilised as a vitamin supplement **[2]**. It is a vitamin D active metabolite that plays a significant role in controlling the calcium balance and bone metabolism **[3-4]**. Early injection of alfacalcidol can safely and beneficially change the normal course of renal bone disease in patients with mild to severe renal failure **[5]**. It shows superior efficacy over ordinary vitamin D with calcium in glucocorticoid-induced osteoporosis, prevention of hip fracture and in the treatment of secondary hyperparathyroidism **[6-10]**. Numerous analytical techniques, such as liquid chromatography, mass spectrometry, high performance liquid chromatography, and Fourier transform infrared spectroscopy, have been reported for the determination of alfacalcidol in bone mass. However, there is no technique that should be simple and time-efficient, so the need for alfacalcidol analysis by a straightforward UV spectrophotometer **[11-13]**.

Alfacalcidol Structure



DRUG PROFILE

Comments	Hydroxylated analog of vitamin D
Chemical Formula	C27 H44 O2
Properties Physical Properties	Colourless to white, odourless crystalline compound; sensitive to heat, light and air; store at 2–8C under nitrogen depending on temperature and time, reversible isomerization to pre-alfacalcidol occurs in solution.
Molecular Weight	400.643
Solubility	Freely soluble in alcohol; soluble in fatty acids; insoluble in water

Human Pharmacokinetics

vitamin D compounds are alfacalcidol (1-hydroxyvitamin D3) is efficiently absorbed from the digestive system, especially when bile salts are present. It is quickly dispersed throughout the body, highly lipid soluble, and readily binds to certain alpha-globulins in blood. About 50% of it is then converted to active 1,25-dihydroxyvitamin D3 by hydroxylation (calcitriol). Before being excreted in bile, the remaining substance likely experiences side-chain oxidative cleavage and 24-hydroxylation. The liver and kidneys are the primary organs involved in alfacalcidol metabolism. Adipose and muscle tissue are significant locations for the long-term storing of vitamin D and its metabolites. Alfacalcidol and other vitamin D molecules are mostly excreted in the bile and faeces, with urine containing very little of them. There is hardly much intact alfacalcidol excreted in the urine or faeces.

Mechanism of action

In condition like chronic renal failure renal bone disease, hypoparathyroidism and vitamin D dependent rickets, the kidney capacity for 1α-hydroxylation is impaired, leading to reduced production of endogenous 1,25-dihydroxyvitamin D and aberrated mineral metabolism. As an active and potent analog of vitamin D, alfacalcidol works to restore the functions and activities of endogenous 1,25- dihydroxyvitamin D.

JOURNAL NAME	REFERENCE	CHROMATOGRAPHIC CONDITION	OBSERVATION
Hindawi Journal of Analytical Methods in Chemistry Volume 2020, Article ID 6201656	Yang Liu *et al*	Column - RP18 column (3.0 mm 150 mm, 3.5 m). Mobile phase - methanol and 0.1% formicacid water in a 1:9 (v/v) ratio. flowrate -0.5 mL/min. The temperatures for the sheath and gas were 11 L/min and 350°C.	The method shows a good linearity with (r 2 > 0.99). Interday and intraday reproducibility was 3.3% and 7.9% [14]
Journal of Applied Pharmaceutical Science Vol. 9(06), pp 021-	22 Dilipkumar Suryawanshi *et al.*	Column - C8 (250 × 4.6 mm) Mobilephase - isocratic elution methanol:acetonitrile (50:50, % v/v) flow rate - 1.0 ml/minutes. Wavelength - 265 nm.	The method was found to be linear (r2 = 0.9993) in the range of 20–100 IU/ml. Limit of detection and limit of quantitation were found to be 10 and 20 IU/ml. The precision, robustness, and ruggedness values were within the acceptance limits (relative standard deviation < 2).

032, June, 2019.			**tablets were found to be 99.89% and 101.46%, respectively [15]**
Brazilian Journal of Development ISSN: 2525-8761	**Luciane Stankiewski*et al*.**	**RP column - C18 mobile phase - isocratic methanol and water (98:2 v/v) a flow rate - 1.2 mL/min UV detection - 265 nm. The retention time - 7.5 min.**	**The method was linear, specific (r=0.9992) interval 10.0 to 80.0 µg/mL, The limit of quantification (LOQ) was 0.52 µg/mL The limit of detection was 0.15 µg/mL. Intermediate precision inter-day - (RSD = 1.13) intra-day - (RSD = 1.16) The accuracy recovery was found to be 102.87 ± 9.84 [16]**
YMER ISSN: 0044-047	**4 Rishu Yadav, Narendra Pandey, Rajiv Kukkar**	**C-18 column mobile phase - 97:3 ratio of methanol and water wavelength - 264 nm flow rate 1.2mL/min**	**The devised approach was found to be linear with a r2 of 0.999 throughout a concentration range of 0.25-1.25µg/mL The mean percentage recovery of Vitamin D-3 were found to be between 95 and 105 percent the LOD and LOQ were determined to be 0.0001 and 0.0005 [17]**
Journal of Chromatography B, 772 (2002) 229–238.	**Tatsuya Higashi, Daisuke Awada, Kazutake Shimada**	**Column 4 µm, 150 X4.6 mm Mobile phase - MeOH and H_2O (19:1, v/v). Flow rate - 1 ml/min Column oven - 40^0C.**	**The intra- and inter-assay coefficients of variation were below 10.6 and 4.7%. The limit of quantitation was 25 pg/ml 3 for a 1.0-ml plasma aliquot**

CONCLUSION

It was concluded from the study that the proposed method was simple, accurate and precise method for the analysis of alfacalcidol in bulk and pharmaceutical tablet dosage form. All the statistical parameters along with recovery data confirm the reproducibility and accuracy of methods. During analysis no interference with the formulation excipients confirms the selectivity as well as specificity of proposed methods. The methods were validated for various other parameters as per ICH guidelines in which they were found to be within the acceptance criteria. Hence the methods can be satisfactorily applied in quality control analysis of alfacalcidol.

REFERENCE

[1] Nash, R.A. & Wachter, A. (2003) Pharmaceutical Process Validation; Published by Marcel Dekker Inc., pp. 507-21.

[2] Nuti, R., G. Bianchi, R. Nuti, G. Bianchi, M.L. Brandi, R. Caudarella, E. D'Erasmo, C. Fiore *et al*. (2006) Rheumatol. Intl. 26: 445-53.

[3] PubChem Compound. 1-hydroxycholecalciferol - Compound Summary (CID 5282181).

[4] Wikipedia. Alfacalcidol. Available at http://en.wikipedia.org/wiki/alfacalcidol.

[5] Hamdy, N.A., J.A. Kanis, M.N. Beneton, C.B. Brown, J.R. Juttmann, J.G. Jordans, *et al*. (1995) BMJ 310: 358-63.

[6] Ringe, J., A. Dorst, H. Faber, K. Ibach & J. Preuss. (2004) Rheumatol. Int. 24: 63-70.

[7] Shiraishi, A., S.Higashi, H. Ohkawa, N. Kubodera, T. Hirasawa, I. Ezawa,

et al. (1999) Calcified Tissue Int. 65: 311-6.

[8] Reginster, J.Y., D. Kuntz, W. Verdickt, M. Wouters, L. Guillevin, C.J. Menkès, *et al*. (1999) Osteoporos Int. 9: 75-81.

[9] Moe, S., L. D. Wazny & J. E. Martin (2008) Can. J. Clin. Pharmacol. 15: 36-43.

[10] Chapuy, M. C., M. E. Arlot, F. Duboeuf, J. Brun, B. Crouzet, S. Arnaud, *et al*. (1992) New Engl. J. Med. 327: 1637-42.

[11] Flann, B. and B. Lodge (1986) J. Assoc. Off. Anal. Chem. 69: 1026-30.

[12] Maunsell, Z., D. J. Wright & S.J. Rainbow (2005) Clinical Chem. 51: 1683-90.

[13] British Pharmacopoeia (2009) Alfacalcidol. Monographs: Medicinal and Pharmaceutical Substances. Available at http://db.yaozh.com/foreign/BP2009/1-2/1-244.pdf.

[14] Liu Y, Chen X, Yuan S, Liu W, He L, Zhang Q. Quantification of Alfacalcidol Tablets Dissolution Content by Chemical Derivatization and LC-MS. Journal of Analytical Methods in Chemistry. 2020 Feb 7;2020.

[15] Suryawanshi D, Jha DK, Shinde U, Amin PD. Development and validation of a stability-indicating RP-HPLC method of cholecalciferol in bulk and pharmaceutical formulations: Analytical quality by design approach. Journal of Applied Pharmaceutical Science. 2019 Jun 5;9(6):021-32.

[16] Stankiewski, L., Toledo, A.C.O., Gonçalves, M.M., Justus, B., Klein, T. and Paula, J.D.F.P., 2021. Development and validation of an RP-HPLC/UV Method for Determination of Cholecalciferol in Polymeric Nanoparticles Suspensions/Desenvolvimento e validação de um método RP-HPLC/UV para determinação do Cholecalciferol em nanopartículas poliméricas Suspensões. Brazilian Journal of Development, 7(2), pp.17955-17967.

[17] Yadav R, Pandey N, Kukkar R. Analytical method development and validation by HPLC for estimation of Vitamin D-3.

[18] Tatsuya Higashi, Daisuke Awada, Kazutake Shimada. Liquid chromatography–mass spectrometric method combined with derivatization for determination of 1a-hydroxyvitamin D in human 3 plasma. 2002 feb 8;229-238.