A COMPREHENSIVE ASSESSMENT OF ANALYTICAL AND BIOANALYTICAL TECHNIQUES FOR QUANTIFYING THE ANTI PROTOZOAL DRUG ORNIDAZOLE

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Abstract

Protozoan and anaerobic bacterial infections are treated with ornidazole, a member of the 5-nitroimidazole medication class, by a mechanism involving preactivation by reduction of the nitro group and formation of harmful derivatives and radicals. Another member of the antibiotic family, metronidazole, has been theorised to interfere with photosynthesis by removing electrons from ferredoxin, which in turn prevents NADP+ reduction and increases radical and peroxide production. Here, we demonstrate a novel method by which ornidazole limits photosynthesis. Ornidazole inhibits the activity of two Calvin cycle enzymes, triose-phosphate isomerase (TPI) and glyceraldehyde-3-phosphate dehydrogenase, while having a negligible impact on the photosynthetic electron transport and oxygen photoreduction (GAPDH). Ornidazole is a C-nitro molecule that is 5-nitroimidazole with 3-chloro-2-hydroxypropyl and methyl groups in place of the hydrogens at positions 1 and 2, respectively. It is employed to treat anaerobic bacterial infections as well as sensitive protozoal infections. It has a role as an antiprotozoal drug, an antiinfective agent, an antibacterial drug, an antitrichomonal drug, an epitope and an antiamoebic agent. It is a member of imidazoles, a C-nitro compound, a secondary alcohol and an organochlorine compound. The molecular weight of $C_7H_{10}ClN_3O_3$ is 219.62 g/mol. Pure ornidazole, dosage forms, biological fluids, and pharmaceutical mixes may be investigated utilizing spectrophotometry, chromatography, electro progressive development, and capillary electrophoretic methods.

The objective of this project is to supply, summarise, and explain the several analytical approaches that may be used to quantify ornidazole either in the their natural form or in mixture with some other active constituents in formulations and biological matrices. These categories essentially group the determinations: (1) volumetric analysis; (2) optical methods; (3) chromatographic techniques; (4) electro analytical methods; (5) capillary electrophoretic; (6) bioanalytical methods; and (7) chemometric analysis.

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1. Optical Methods

UV/ visible spectrophotometric methods

Spectrophotometry measures a material's reflecting or transmitting qualities as a function of wavelength. Spectrophotometric approaches for drug testing can be utilized in quality control labs without expensive equipment like GLC or HPLC. These methods are simple, cheap, and time-efficient.

Precision was calculated as repeatability and intra and inter day variations (% RSD) for both the drugs. Optical characteristics and summary of validation parameters for method is given in Table 1. By observing the validation parameters, the method was found to be simple, sensitive, accurate and precise. Hence the method can be employed for the routine analysis of these two drugs in combined synthetic mixture Precision was calculated as repeatability and intra and inter day variations (% RSD) for both the drugs. Optical characteristics and summary of validation parameters for method is given in Table 1. By observing the validation parameters, the method was found to be simple, sensitive, accurate and precise. Hence the method can be employed for the routine analysis of these two drugs in combined synthetic mixture

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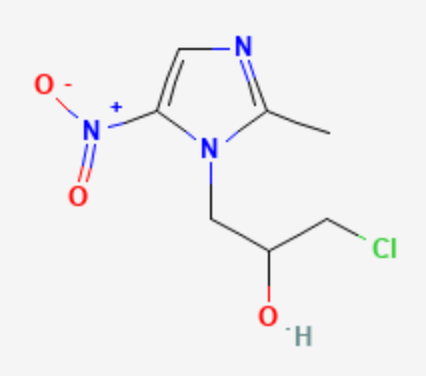
Figure 1: Chemical structure of Ornidazole (ORN)



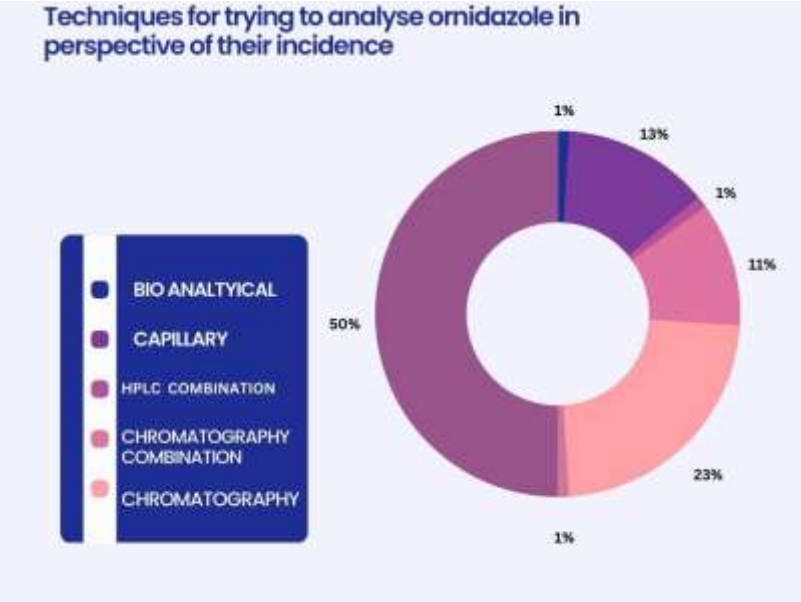


Figure.2 Techniques for trying to analyse ornidazole in perspective of their incidence Database sources: Science direct, Elsevier, Web of science, Springer, Taylor and Francis, Scopus and PubMed

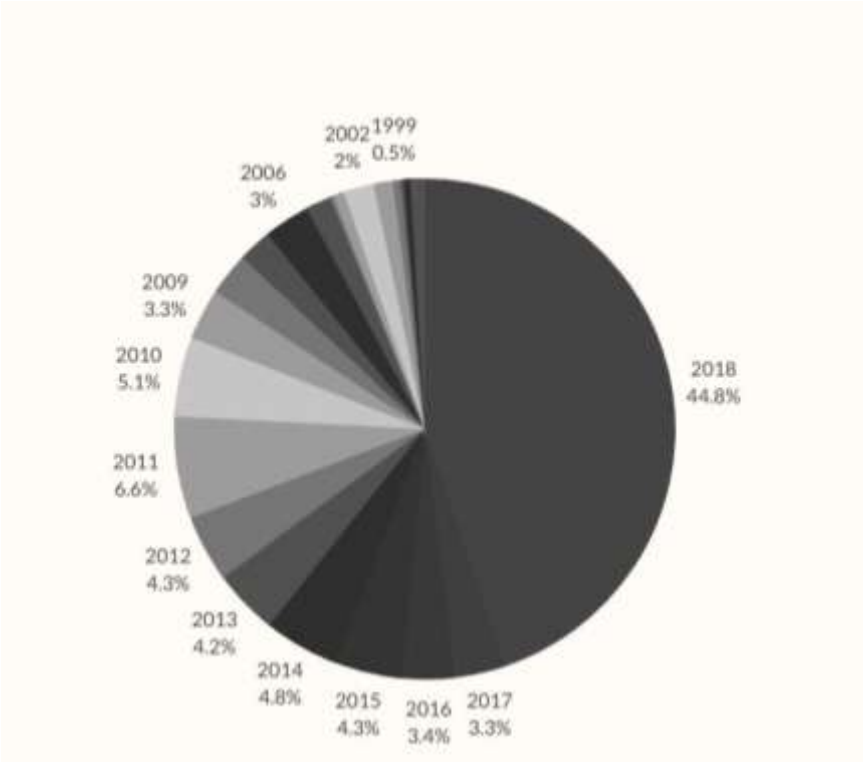


Figure 3: ornidazole annual publication

SPECTROPHOTOMETRY COMBAINED									
ANALYTE	METHOD	MATRICES	SOLVENT	DETECTION WAVELENGHT(nm)	LINEARITY	LOD	LOQ	CORRELATION COEFFICIENT	REF
CEF, ORN	UV spectrophotometric simultaneous equation	combined tablet dosage form	Methanol and water	CEF-288nm ORN -320nm	f 2-30 µg/mL	NIL	NIL	0.998 and 0.999	11
OFLAXACIN , ORNIDAZOLE	UV spectrophotometric simultaneous equation	binary mixture		288 nm ofloxacin and 322 nm for ORN	2.0-10.0 µgml-1				12
ORN	UV Spectrophotometric method	ORN tablets	eutectic liquid of phenol and lignocaine hydrochloride)	319 nm				0.9993	33
Levofloxacin Hemihydrate and Ornidazole	UV spectrophotometric	combined	deionized water	Levo shows λmax at 288	1-11 µg/mL for	0.9981	0.9969	0.9993	40

	method for the simultaneous estimation	dosage form		nm and orni at 317 nm	levo and 2-22 µg/Ml for ORNI				
doxycycline monohydrate and ornidazole	Simultaneous spectrophotometric determination	bulk and pharmaceutical formulation	methanol	311.4 nm	3-27 µg/mL			N/A	54
ornidazole	differential UVspectrometric method	bulk and pharmaceutical formulation	deionized water	322 nm	8-20µg/mL	N/A	N/A	N/A	60
cefixime and ornidazole	Spectrophotometric analysis	binary mixture	ethanolic solns	318.6 nm and 277 nm	4.0-20.0 µgml-1 cefixime and 6.0-30.0 µgml-1 ornidazole		0.9969	0.9993	50
ornidazole and diloxanide furoate	uv spectrophotometric method	bulk drug and combined dosage form		311 nm as λmax for Ornidazole and 258 nm as λmax for DF	f 2.5 - 7.5 µg/mL and 3.25 - 11.25 µg/mL	0.9981	0.9969	0.9993	45
levofloxacin & ornidazole	Spectrophotometric & RP-HPLC method	tablet dosage form	Acetonitrile : 0.05% Ortho-phosphoric acid in water	293.5nm and 318nm	4 -20 µg/mL and 8-40 µg/mL for LEVO and OZ				37
ornidazole and curcumin	spectrometric simultaneous estimation	dosage forms loaded with synthetic and herbal drug combination	ethanol	319 nm and 430 nm	1 to 10 µg/mL	0.9981	0.9969		41
ornidazole and chloranilic acid	spectrophotometry		propanol		3.0-83 mg/L			0.9993	42
ORN	spectrophotometric method	pure and pharma	naphtoL	521.5 nm	15 µg.ml -1	0.9981	0.9969		

		ceutical formulations							
5-nitroimidazoles and ORN	UV Spectrophotometric method	tablet dosage form	0.5% sulfanilamide and 0.3% NEDA.	540nm					
Ciprofloxacin and Ornidazole	UV Spectrophotometric method	tablet dosage form		302.5 nm and 335 nm	2-10 µg/mL and 2-20 µg/mL				

spectrofluorimetric method
The extensive usage of spectrofluorimetry in quality control settings may be attributed to its portability, reliability, and flexibility of use. ORN were isolated via spectrophotometric methods, either or in association with other pharmaceuticals.
Chromatographic methods

HPLC
To segregate chemical mixtures empirically, HPLC is the benchmark. LC has good sensitivity, endurance, and precise. The method was validated for linearity, precision, recovery, specificity, limit of detection, limit of quantification and robustness. The linearity was obtained in the concn. range of ornidazole with mean recovery of 99.87 ± 1.10 making it simple and sensitive method useful for the routine quality control testing of ciprofloxacin and ornidazole combined pharmaceutical dosage forms.

Planar chromatography (TLC)
A breakthrough is high-performance thin-layer chromatography (TLC). TLC resolution improves increasing automation, and so does quantitative data integrity. HPTLC can analyse several samples with minimal to no solvent. Analyzing, exposing, and disposing of hazardous organic effluents is less affordable, leading in less pollution to the environment. We provide HPTLC methods for determining ORN concentrations in pure form as well as in medicines. Classical chromatography is enhanced by high performance thin-layer chromatography (TLC). TLC resolution increases with automation, as does quantitative information quality. Due to its high throughput and low solvent demands, HPTLC was appropriate for swiftly analysing a large amount of samples. Less money is spent on analysing, exposing, and disposing of hazardous organic effluents, which is good for the environment. The following are HPTLC techniques for detecting PHE in isolation and in medicaments.

Electroanalytical methods
Practitioners apply titration, spectrometry, chromatography, and immunoassays. Transmitting heavy, specialized analytical undertaking this project bedside measurements difficult and moment. Electroanalysis is efficient, sensitive, and expense. Electroanalysis may evaluate ORN alone or in mixture

Capillary electrophoretic methods
HPLC results was utilized to construct a capillary electrophoresis (CEs) technique. CE is preferable than HPLC for distinguishing biomolecules. Electrophoresis and electrochromatography are often used together. Capillary electrophoresis of ORN By Al Azzam ET AL., proposed and successfully applied to the assay of enantiomers of both ofloxacin and ornidazole in pharmaceutical formulations. The computational calculations for the enantiomeric inclusion complexes rationalized the reasons for the different migration times between the ofloxacin and ornidazole enantiomers.

Bioanalytical Methods
Direct measurements must be made of biological events. Response observed to be linear in the concentration range of 100-500 ng/band for both cefuroxime axetil and ornidazole was proposed by Poonam N. Ranjane et al. With a percentage accuracy of 102%, the technique has been successfully used for drug analysis in pharmaceutical formulation.

Chemometrics
Stacking spectra precludes identification of the active medicinal component in formulations and biological fluids. Numerical and graphical algorithms correct the original absorption spectra. Gui, Yi; Ni et al, used chemometrics to resolve the overlapped voltammogram and quantify the mixtures. The proposed method was successfully applied to the determination of three 5-nitroimidazoles in milk and honey samples

2. Discussion

ORN has been utilized in drug manufacturing, UV/VIS spectroscopy, and HPLC. Liquid chromatography is frequently used for both solitary and combined ORN analysis.Recent advances in ORN determination have been hindered by the need to upgrade sophisticated equipment to strengthen sensitivity and tackle issues such the cost-effective use of organic solvent in sample preparation.

3. Conclusion

This research is aimed at spectrophotometric and spectrofluorimetric chromatographic characterization of ORN in both standalone and in combination with other drugs, following its evolution and development through time. Liquid chromatography is frequently used for both solitary and combined ORN analysis. Though there are established protocols for determining and managing ORN levels, most procedures still do not adhere to environmentally benign principles. Therefore, efforts will be made to create biological matrices and dosage forms that limit negative impacts on the environment. As a result, less potentially harmful organic effluents are needed.

4. Reference

Phatak, Hetal; Vaidya, Vikas et al., A rapid gas chromatography- mass spectroscopy method for simultaneous quantification of ornidazole and miconazolef rom cream formulations: development, validation and application: International Journal of Pharmaceutical Sciences and Research (2016), 7(7), 2976-2983. DOI:10.13040/ijpsr.0975-8232.7(7).2976-83

Kumaraswamy, Damerakonda; Phanidra, et al., A Estimation of ciprofloxacin and ornidazole by UV-spectroscopy, RP-HPLC and their application in pharmacokinetic studies.; International Journal of Pharmacy and Technology (2016), 8(2), 13578-13591.

Rele, Rajan V.; Sawant, Swapnil A et al., Simultaneous spectrophotometric estimation of ofloxacin and ornidazole by first order derivative spectroscopy method in combined dosage form, Chemica Sinica (2013), 4(4), 43-48, 6

Swamiappan, Yamuna; Arcot, Shantha et al.,Simultaneous spectrophotometric determination of cefixime and ornidazole in pharmaceuticals by chemometric methods, Inventi Impact: Pharm Analysis & Quality Assurance (2013), (1), 38-42

Rege, P. V.; Sathe, P. A. et al., A simple electro analytical method for estimation of ofloxacin and ornidazole individually from pharmaceutical formulation By Salvi, V. S. International Journal of Pharmaceutical Research (2011), 3(4), 9-12.

Ma, Yunsu; Wang, Qianru; Zhang, Hongwen; Xie, et al., Simultaneous quantification of antofloxacin and its major metabolite in human urine by HPLC-MS/MS, and its application to a pharmacokinetic study, Biomedical Chromatography (2017), 31(9), DOI:10.1002/bmc.3962

Veena, K.; Sireesha, D. et al., Analytical method development and validation for the simultaneous estimation of cefixime trihydrate and ornidazole in combined dosage form by RP-HPLC method , Indo American Journal of Pharmaceutical Research (2015), 5(10), 3128-3134.

Alzoman, Nourah Z et al., A validated stability-indicating and stereoselective HPLC method for the determination of lenalidomide enantiomers in bulk form and capsules. Journal of Chromatographic Science (2016), 54(5), 730-735. DOI:10.1093/chromsci/bmv247

Yuan, Xiao-wei; Sun, Ting-ting et al., Determination of dextroisomer in S-ornidazole substances by HPLC, Shenyang Yaoke Daxue Xuebao (2015), 32(8), 609-611, 617. DOI:10.14066/j.cnki.cn21-1349/r.2015.08.005

Dewani, Anil P.; Bakal, Ravindra L.et al., Development of a single ion pair HPLC method for analysis of terbinafine, ofloxacin, ornidazole, clobetasol, and two preservatives in a cream formulation: application to in vitro drug release in topical simulated mediaphosphate buffer through rat skin, Journal of AOAC International (2015), 98(4), 913-920. DOI:10.5740/jaoacint.14-189

Srilekha, A.; Pavani, P.; Sreedhar, B et al., Stability indicating RP-HPLC method development and validation for simultaneous estimation of doxycycline monohydrate and ornidazole in bulk and pharmaceutical dosage form, International Journal of Pharmaceutical Sciences and Research (2015), 6(5), 2228-2239. DOI:10.13040/IJPSR.0975-8232.6(5).2228-39

R.; Patel, U. M.; Patel et al., Development and validation of stability indicating RP-HPLC assay method for cefixime trihydrate and ornidazole in bulk drug and combined tablet dosage form, International Journal of Pharmaceutical Research and Bio-Science (2014), 3(3), 326-342.

Jain, Surendra Kumar; Singh, Meena; Jain, Ruchi et al., Spectrophotometric & RP-HPLC method development and validation for simultaneous estimation of levofloxacin &

ornidazole By Jain, Nilesh, International Journal of Pharmaceutical Sciences and Research (2014), 5(8), 3370-3377. DOI:10.13040/IJPSR.0975-8232.5(8).3370-77

Analytical method development and validation for simultaneous estimation of cefixime trihydrate and ornidazole in tablet dosage form by RP-HPLC By Babu, J. Ramesh; Vidyadhara, S.; Anusha, V. From Biosciences, Biotechnology Research Asia (2012), 9(2), 781-787. Language: English, Database: CAPLUS, DOI:10.13005/bbra/1064

Du, Jiangbo; Deng, Pan; Chen, Xiaoyan et al., Characterization of ornidazole metabolites in human bile after intravenous doses by ultraperformance liquid chromatography/quadrupole time-of-flight mass spectrometry; Acta Pharmaceutica Sinica B (2012), 2(2), 159-167, DOI:10.1016/j.apsb.2012.01.002

Sun, Yi; Tian, Ajuan; Wang,et al., Impurity detection method and content detection method of ornidazole injection using HPLC Faming Zhuanli Shenqing (2012), CN 102539564 A 20120704,

Ahmadi, Moahammad Bashir; Doshi, Divyeshkumar B et al., Simultaneous estimation of cefixime trihydrate and ornidazole by high performance thin layer chromatography method,Journal of Chemical and Pharmaceutical Research (2015), 7(7), 547-552.

Aher, Smita S.; Saudagar, et al., Development and validation of HPTLC method for the simultaneous estimation of cefixime trihydrate and ornidazole in tablet dosage form World Journal of Pharmaceutical Research (2014), 3(6), 592-601.

Patel, Satish A.; Patel, Natvarlal J. et al., Development and validation of HPTLC method for simultaneous estimation of levofloxacin and ornidazole in tablet dosage form , Journal of Pharmaceutical Education and Research (2011), 2(2), 78-83.

Patel, Satish A.; Patel, Natvarlal J. Development and validation of HPTLC method for simultaneous estimation of levofloxacin and ornidazole in tablet dosage form Journal of Pharmaceutical Education and Research (2011), 2(2), 78-83.

Patel, S. A.; Patel, N. J. Development and validation of HPTLC method for simultaneous estimation of ciprofloxacin and ornidazole in tablet dosage forms]ournal of Pharmaceutical Research (2011), 10(4), 159-162.

Puranik, Manisha; Bhawsar et al., Simultaneous determination of ofloxacin and ornidazole in solid dosage form by RP-HPLC and HPTLC techniques Indian Journal of Pharmaceutical Sciences (2010), 72(4), 513-517. DOI:10.4103/0250-474X.73937

Ranjane, Poonam N.; Gandhi, Santosh V , HPTLC Determination of Cefuroxime Axetil and Ornidazole in Combined Tablet Dosage Form journal of Chromatographic Science (2010), 48(1), 26-28, DOI:10.1093/chromsci/48.1.26

Surendra, K.; Mageswari, S. D.; Maheswari, R.et al., Simultaneous estimation of levofloxacin hemihydrate and ornidazole in tablet dosage form by HPTLC. Asian Journal of Chemistry (2007), 19(7), 5647-5651.

Chepurwar, S. B.; Shirkhedkar, A. eta l., Validated HPTLC method for simultaneous estimation of levofloxacin hemihydrate and ornidazole in pharmaceutical dosage form Journal of Chromatographic Science (2007), 45(8), 531-536. DOI:10.1093/chromsci/45.8.531

Sreekanth, N.; Shivshanker, K.et al.,Simultaneous determination and validation of ornidazole and cefixime by HPTLC in pure and pharmaceutical dosage forms,Asian Journal of Chemistry (2007), 19(5), 3621-3626.

Sreekanth, N.; Shivshanker, K.; Determination of gatifloxacin and ornidazole in tablet dosage forms by high-performance thin-layer chromatography,Analytical Sciences (2006), 22(5), 743-745. DOI:10.2116/analsci.22.743

Puranik Manisha; Bhawsar D V,Simultaneous Determination of Ofloxacin and Ornidazole in Solid Dosage Form by RP-HPLC and HPTLC Techniques, Indian journal of pharmaceutical sciences (2010), 72(4), 513-7,

Swamiappan, Yamuna; Arcot, Shantha et al.,Simultaneous spectrophotometric determination of cefixime and ornidazole in pharmaceuticals by chemometric methods Inventi Impact: Pharm Analysis & Quality Assurance (2013), (1), 38-42.

Gui, Yi; Ni, Yong-Nian; Kokot et al.,Simultaneous determination of three 5-nitroimidazoles in foodstuffs by differential pulse voltammetry and chemometrics ,Chinese Chemical Letters (2011), 22(5), 591-594. DOI:10.1016/j.cclet.2010.12.014

Varun, G.; Shyamkumar, B.; Cylma, et al., Development of RP-HPLC method for the quantitative estimation of ofloxacin and ornidazole in combined liquid oral dosage forms, International Journal of Pharmaceutical Sciences and Nanotechnology (2013), 6(1), 1972-1976, 5

Babu, J. Ramesh; Vidyadhara, S.; Anusha, V et al., Analytical method development and validation for simultaneous estimation of cefixime trihydrate and ornidazole in tablet dosage form by RP-HPLC, Biosciences, Biotechnology

Research Asia (2012), 9(2), 781-787. DOI:10.13005/bbra/1064

Sun, Ya-xin; Zhu, Xu; Qiu, Feng; Ion-pairing RP-HPLC determination of ornidazole in human plasma From Zhongnan Yaoxue (2012), 10(12), 896-898. DOI:10.3969/j.issn.1672-2981.2012.12.005

Khattab, Fatma I.; Ramadan et al., Stability-indicating methods for the determination of Ornidazole in the presence of its degradate according to ICH guidelines Pharmaceutica Analytica Acta (2012), 3(8), 1000179/1-1000179/8. DOI:10.4172/2153-2435.1000179

Xie, Li; Zhao, Shu-wen; et al.,Determination of related substances in ornidazole injection by HPLC , Huaxi Yaoxue Zazhi (2012), 27(4), 441-442.

Et al., Wei, Chunyan; Wang, Wendi; Liang, Yanfang;Determination of 2-methyl-5-nitroimidazole in ornidazole injections by HPLC, Zhongguo Yaoshi (Wuhan, China) (2012), 15(9), 1291-1293.

Chandorkar, J. G.; Pande, V. V.; Dongare, et al., A sensitive HPLC method of determination of 2-methyl 5-nitro imidazole & reaction mass of intermediates of ornidazole in ornidazole bulk manufacturing,International Journal of Engineering Research and Industrial Applications (2012), 5(3), 145-149

Govind J.; Ram, Vijay R.; Pandiya et al.,Validated LC method for simultaneous analysis of Cefixime and Ornidazole in commercial tablets, International Journal of ChemTech Research (2012), 4(3), 1124-1136.

Sun, Yi; Tian, Ajuan; Wang, Jie et al., Impurity detection method and content detection method of ornidazole injection using HPLC, Faming Zhuanli Shenqing (2012), CN 102539564 A 20120704.

Shravan Kumar, A.; Santhosh Kumar, T.; Kalyan Kumar, B.et al.,Development and validation of RP-HPLC method for simultaneous estimation of levofloxacin and ornidazole in pharmaceutical dosage form , Journal of Pharmacy Research (2011), 4(11), 3864-3866, 3

Shravan Kumar, A.; Santhosh Kumar, T.; Kalyan Kumar, B et al., Development and validation of RP-HPLC method for simultaneous estimation of moxifloxacin and ornidazole in pharmaceutical dosage form , Journal of Pharmacy Research (2011), 4(11), 3864-3866, 3

Simultaneous estimation of cefixime trihydrate and ornidazole in combined tablet dosage form by RP-HPLC By Patel, Jaimin; Joshi, Smita From Journal of Chemical and Pharmaceutical Research (2012), 4(4), 2167-2172. Language: English, Database: CAPLUS

Patel, Keyur M.; Zanwar, Aarti; Sen et al., Simultaneous estimation of Levofloxacin hemihydrate and Ornidazole in tablet dosage form by using simultaneous equations method Pharma Science Monitor (2012), 3(1), 59-66.

Patel, Satish A. et al., Development and validation of RP-HPLC method for simultaneous determination of ciprofloxacin and ornidazole in tablets, International Journal of Current Pharmaceutical Research (2011), 3(4), 72-75.

Rege, P. V.; Mapari, Ramesh , Simultaneous quantification of ofloxacin and ornidazole from combined pharmaceutical drug formulation by HPLC,International Journal of Pharma and Bio Sciences (2011), 2(4), 51-58.

Nalini, C. N.; Ramachandran, S.; Simultaneous determination of ofloxacin and ornidazole in tablets by spectrophotometry and reverse phase HPLC , Research Journal of Pharmaceutical, Biological and Chemical Sciences (2011), 2(3), 693-708.

Sudhakar, M.; Venkateshwara Rao, J.; Devika, G. A validated RP-HPLC method for simultaneous estimation of cefixime trihydrate and ornidazole in tablet dosage forms. International Journal of Chemical and Pharmaceutical Sciences (2010), 1(2), 34-39.

Zhao, Dongmei et al., Determination of metronidazole and ornidazole by RP-HPLC ,Shanxi Yiyao Zazhi (2011), 40(2a), 196.

Sahoo, Bijay Kumar; Mukherjee et al., Development and validation of a high-performance liquid chromatographic method for bioanalytical application with Ranitidine HCl ,International Journal of Pharmacy and Pharmaceutical Sciences (2011), 3(Suppl. 2), 34-38.

Anbarasi, B.; Seetharaman, R.; Suresh, V.et al., Analytical method development and validation of simultaneous RP-HPLC estimation of ornidazole and ofloxacin in tablet dosage forms , Journal of Pharmacy Research (2011), 4(1), 272-273.

Vinod Kumar, K.; Dharuman, J.; RP-HPLC method development and validation for simultaneous estimation of sulbactam and cefoperazone in dosage form and in plasma,International Journal of Pharma and Bio Sciences (2010), 1(4), 87-92.

Varun, G.; Shyamkumar, B.; Cylma, M et al., Development of RP-HPLC method for the quantitative estimation of ofloxacin and ornidazole in combined liquid oral dosage forms ,International Journal of Pharmaceutical Sciences and Nanotechnology (2013), 6(1), 1972-1976, 5

Babu, J. Ramesh; Vidyadhara, S.et al., Analytical method development and validation for simultaneous estimation of cefixime trihydrate

and ornidazole in tablet dosage form by RP-HPLC, Biosciences, Biotechnology Research Asia (2012), 9(2), 781-787. DOI:10.13005/bbra/1064

He, Jia-jia; Zhu, Pei-xi; et al., Characterization of major impurity in ornidazole and sodium chloride injection,Yaowu Fenxi Zazhi (2012), 32(10), 1822-1825.

Gandhi, V. M.; Nair, S. B.; Menezeset al., Development of UV-spectrophotometric method for the quantitative estimation of Ofloxacin and Ornidazole in combined liquid oral dosage form by simultaneous equation method, International Journal of Research in Pharmacy and Chemistry (2013), 3(1), 6-11.

Khattab, Fatma I.; Ramadan, Nesrin K et al.,Stability-indicating methods for the determination of Ornidazole in the presence of its degradate according to ICH guidelines, Pharmaceutica Analytica Acta (2012), 3(8), 1000179/1-1000179/8. DOI:10.4172/2153-2435.1000179

Xie, Li; Zhao, Shu-wen; Determination of related substances in ornidazole injection by HPLC; Huaxi Yaoxue Zazhi (2012), 27(4), 441-442.

Chandorkar, J. G.; Pande, V. V.; Dongare, M. K.; A sensitive HPLC method of determination of 2-methyl 5-nitro imidazole & reaction mass of intermediates of ornidazole in ornidazole bulk manufacturing International Journal of Engineering Research and Industrial Applications (2012), 5(3), 145-149.

Sharma, Rajesh; Pathodiya, Geetam; Mishra, Ganesh Prasad et al., Simultaneous estimation and validation of Cefixime trihydrate and Ornidazole in combined solid dosage form using hydrotropic solubilizing agent,Novel Science International Journal of Pharmaceutical Science (2012), 1(8), 589-594.

Kher, Govind J.; Ram, Vijay R.; et al.,Validated LC method for simultaneous analysis of Cefixime and Ornidazole in commercial tablets, International Journal of ChemTech Research (2012), 4(3), 1124-1136.

Grewal, A. S.; Bhardwaj, S. K.; Patro et al.,Visible spectrophotometric estimation of ornidazole in pure and pharmaceutical formulation, International Journal of ChemTech Research (2012), 4(3), 1044-1048.