Modern chromatographic method for estimating Loratadine and affections on healthcare

H.N.K. Al-Salman, Qutaiba A. Qasim, Rajaa Hussein Fayadh and Hussein H. Hussein

Abstract

Purpose – *The purpose of this study is to establish Loratadine [LRD] quantification in purified and capsule formulations using a precise and specific Reversal Phase with a very high-performance liquid Chromatographic [RP-HPLC] technique. The approach was evaluated in agreement with the principles of the International Conference on Harmonization [ICH]. Arcus EP-C18 Ion Pac column, 5 m, 4.6 mm, 250 mm, mobile phase Methanol: Acetonitrile (60:40) v/v. Dibasic potassium phosphate buffer, pH 7.2, flow rate 1.0 ml/min.*

Design/methodology/approach – *The HPLC system used a 340 nm UV detector for testing. A 10-min run time was used for the analysis. At concentrations ranging from 2 to 10 g/ml, the technique was linear (R^2 = 0.9998), exact (intra-day and inter-day relative standard deviation [RSD] values 1.0%), accurate (range recovery = 96%–102%), exclusive and strong.*

Findings – *The detecting and quantitation limits were 0.92 g/ml and 2.15 g/ml, respectively.*

Originality/value – *The findings demonstrated that the proposed method could accurately determine LRD in bulk and pill dose formats quickly and accurately.*

Keywords *Health care, Loratadine degradation, RP-HPLC- LC100, Loratadine drug [LRD]*

Paper type *Research paper*

1. Introduction

[ethyl 4–(13-chloro-4-azatricyclo [9.4.0.0]pentadeca-1(11),3(8),4,6,12,14-hexaen-2-ylidene) piperidine-1-carboxylate], $C_{22}H_{23}ClN_2O_2$, Mol.Wt.382.89 g mol^{-1}) (Council of Europe, 2013).

Loratadine (LRD) is an acetonitrile crystalline. At a temperature of about 133°C–136°C, the sample has a melting point of 134°C–136°C and appears in Figure 1.

Loratadine is an antihistamine that is sold underneath the brand names Claritin and many others. Hay fever and hives are examples of allergic rhinitis. Loratadine/pseudoephedrine is a mixture of loratadine and pseudoephedrine, a decongestant. It is administered orally (Palade *et al.*, 2013; Bîrsan *et al.*, 2014). Sleepiness, dry mouth and headache are all commonly prescribed drugs. Adverse reactions, convulsions and liver issues are among the more serious adverse effects.] Although it looks to be completely risk-free, there has not been much research done on it. It is not suggested for youngsters under the age of two. It relates to the second-generation antihistamine class of medicines. After becoming invented in 1980, loratadine was first launched in the market in 1988. The World Health Organization classifies it as a critical resource. Loratadine is a generic medication that is marketed. In the USA, it is available over-the-counter. The 76th most usually reported medicine in the USA in 2018, with over 10 million procedures performed (Khan *et al.*, 2013; Fayadh *et al.*, 2021).

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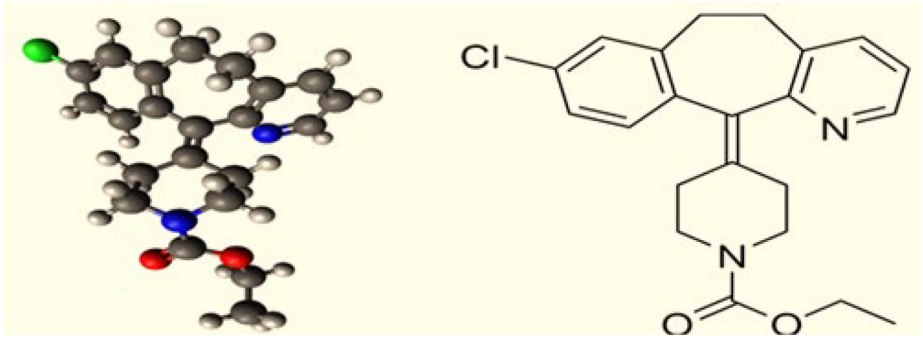
Authors' contributions: this study was carried out independently at the laboratories of the University of Basrah's College of Pharmacy. This study was done over the course of three months with serious and constant effort, yielding outstanding results in terms of identifying a simple and sensitive approach for estimating the LDR.

Figure 1 Chemical structure of Loratadine



1.1 Synthesis of LRD

The loratadine intermediates are made by mixing 3–20 wtper cent P2O5 into polyphosphoric acid ester and mixing at 175˚C–240˚C to achieve a homogenous environment; then mixing 3-[2–(3-chlorophenyl) ethyl] 4–16 wtper cent-2-pyridyl formonitrile into the mixture and reaction at 175–240 deg. Moreover, loratadine was synthesized by converting N-methyl piperidine for equivalent ethyl carbamate (6.1. 3) – loratadine was synthesized in the very identical method: by refluxing chloroformate in toluene (Hydrotropicsolubilisation Phenomenon, 2015), as shown in Figure 2.

2. Goal of the study

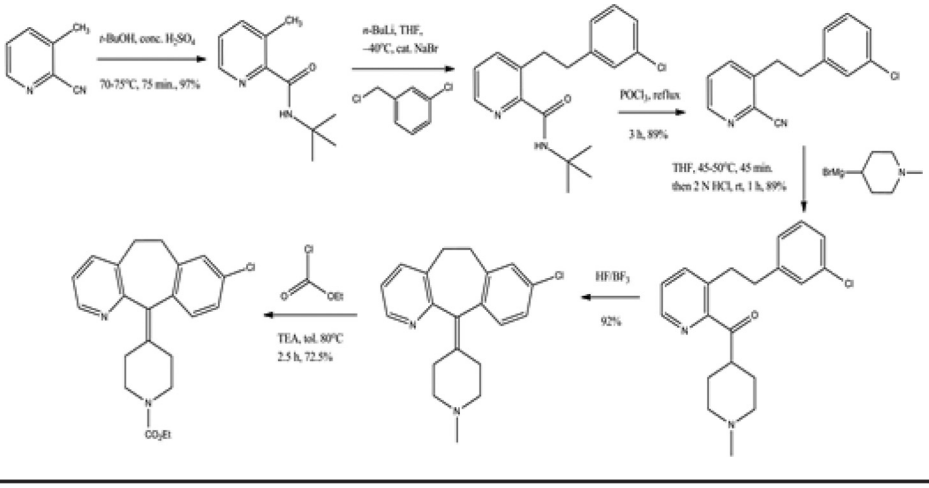
The goal of the study was to build and validate an RP-HPLC method including an ultraviolet (UV) detector for quantitatively assessing LRD in pharmaceuticals.

3. Experimental

3.1 Instrumentation

Completely automated digital computer management is standard on the LC-100 series S-HPLC. Its electrical circuit architecture, internal electrical design approach, process

Figure 2 Synthesis of Loratadine



optimization, cinematography workspace capabilities and performance characteristics make it one of the most stable and reliable instruments available. The LC100-type HPLC-UV comprises a dual-beam optical spectrometer (Angstrom Advanced Inc. USA); an IBM-compatible PC is attached to a UV-100 PC, which is approximately one-centimeter-long equipped with a quartz cell with a light frequency of 100 UV. It was an utterly PVC imitation. The PLS Toolbox is used in conjunction with the VP pumps and variable frequency with Matlab R2003b. reconfigurable UV determinants were impressive. PLS Toolbox works with Matlab R2003b for this project. Chemometric approaches and the PLS (halfway least squares) were fantastic with PLS Toolbox used with The R2003b version of Matlab, VP pumps and changeable voltage computer-controlled UV indicator. An Angstrom Advanced Inc. LCL solution programming program was used to organize peak areas. The chromatographic separation and measurements were carried out on an Ion Pac section with an ArcusEP-C18 analytical column (250 mm 4.6 mm; molecule size 5 m) maintained at room temp. Drug reference and tablet test setups were screened through a millipore layer channel in the mobile phase before being injected into the HPLC framework (Pani *et al.*, 2014; Ponnilavarasan, 2011; Pavalache, 2011; Shalini and Sahoo, 2014; Sujatha and Balmuralikrishna, 2014).

3.2 Chemicals and reagents

3.2.1 Pure standard. Standard LRD for medical equipment and medicines with stated purity of 99%, depending on the company's factory certification and granted by Industrial Pharma Alfayhaa®Iraq under NO. LRHB0542.

3.2.2 Market sample. India's LRD–Lincolin-LPL® pharma-tablets, Batch No. RJ8003, code No. GUJ/DRUG/G-1419, contain five mg each tablet.

3.2.3 Configure the samples for measurement.

- Sigma-Aldrich® HPLC grade solutions.
- To produce a 1 mg/ml LRD concentration, one-of-a-kind sample was produced in Methanol: Acetonatrile (60:40) v/v. dibasic potassium phosphate buffer, pH 7.2.
- To generate the concentrations of (2, 4, 6, 8 and 10) g/ml, LRD (standard solution) was produced in Methanol: Acetonatrile (60:40) v/v. dibasic potassium phosphate buffer, pH 7.2.

3.2.4 Sample modernization. The simplified PLS alignment set was increased using numerous samples of LRD - Lincoln-LPL®, India, pills having experienced sums from regular LRD −5 mg tablets to conduct samples Upgrading. One known focus to three obscure interrelationships of evaluations comprising specific classifications with each must have been introduced purpose for complete the fundamental improvement as well as insightful potential, a consequence of rejuvenated example was inspected using external acceptance tests (Hasan *et al.*, 2021; Kwekha-Rashid *et al.*, 2021), at a particular theme figure out how to mission defines refreshing as well as section implementing the developed strategy RP-HPLC with three concentrations regarding increased refreshing (Abu-Rumman, 2021; Abu-Rumman *et al.*, 2021).

4. Procedure

4.1 Standard drug solution

Standardized configurations were planned using the solvent system as a solvent dispersing an accurately calibrated amount of LRD (50 mg) in 100 ml of the versatile stage in a 250 ml volumetric flask gives you an approximately 50:50 mixture of liquid nitrogen and LRD. a standard stock configuration of LRD (500 g/ml) was created. The transportable step was then used to make the cup adequate. To set up the development standards configurations

Table 1 Considerations of RP-HPLC technique

Mobile phase	*Methanol: Acetonatrile (60:40)v/v. dibasic potassium phosphate buffer, at pH 7.2*
Flow rate	1.0 ml/min
Detection wavelength	340 nm
Column temperature	30°C
Injection volume	20 μL
Run time	10 min

of LRD (2, 4, 6, 8 and 10) g/m (Ramulu *et al.*, 2011), the stock arrangement was attenuated appropriately with the portable stage.

4.2 Chromatographic conditions

The results of the main guidelines acquired using the reverse-phase chromatography technology are shown in Table 1 (RP-HPLC).

4.3 Calibration curve

The suggested strategies and tactics alignments bending were created for LRD over such a range of concentrations (2, 4, 6, 8 and 10) g/ml. The three-fold configuration was produced, and 20 l of each combination was pumped onto the segment. At 400 nm, the pinnacles became defined. Planning the pinnacle region versus focus yielded the LRD modification bend (Pavalache *et al.*, 2010).

4.4 Exertion degeneration studies (Al-Salman *et al., 2020a*; Al-Salman *et al., 2020b*; United States of Pharmacopoeia, *2007*; ICH Harmonized-Tripartite Guidelines, *2005*; Walash *et al., 2011*; Youssef *et al., 2012*; Pavalache *et al., 2010*; Sujatha *et al., 2014*)

Different ICH-recommended stress settings, such as acidic, basic, oxidative, warm and photolytic effort, were used in the effort degradation experiments.

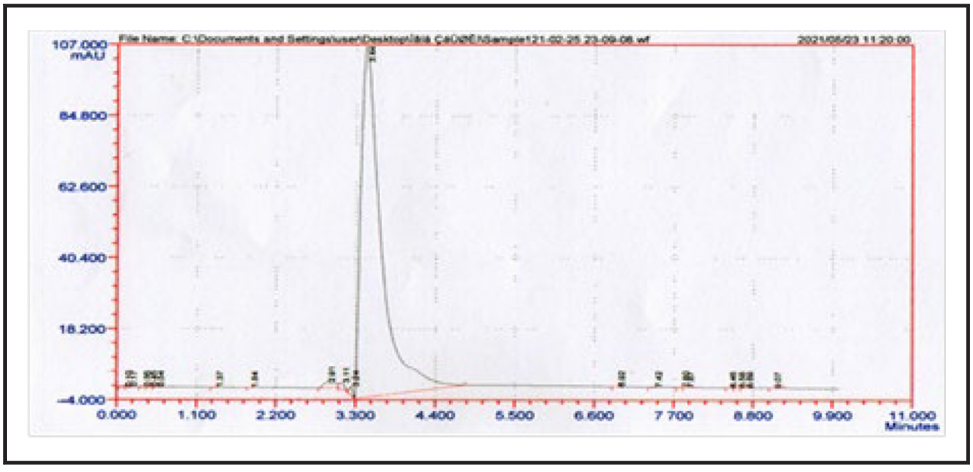
4.4.1 Acid degeneration. In a 100 ml volumetric glass, 60 mg of LRD tablet powder was ingested. Each jar was filled with 5 ml of 0.1 N HCl and held at 70˚C–80˚C in a reflux state for 2–3 h. Because after the intensity was reached, the structure was destroyed with 0.1 N NaOH, and the flexible stage was used to complete the fight. Hydrochloric acid may be used to hydrolyze LRD. Hydrolysis, or hydrogen generation, is one such reaction. Any acid or base stimulates amine hydrolysis (Figure 3).

4.4.2 Base degeneration. When using bases to inhibit amines, such as NaOH or potassium hydroxide, the outcome is amine salt. In a 100 ml volumetric decanter, 60 mg of LRD tablet powder was taken. The container was filled with 5 ml of 0.1 N NaOH and held at 70˚C–80˚C in a reflux setting for 2 to 3 h. After being brought to maximum pressure, the structure was destroyed with 0.1 N HCl and had concluded sufficiently using a flexible phase (Figure 4).

4.4.3 Oxidative degeneration. In a 100 ml volumetric flask, 60 mg of LRD tablet powder and 5 ml of 20% H2O2 were combined. For 2–3 h, the flask was maintained at 70˚C–80˚C in a rotary evaporator. The jar was finished sufficiently with the movable phase after the pressure conclusion (Figure 5).

4.4.4 Photolytic degeneration. LRD e tablet powder (60 mg) was placed on the glass Petri plate and subjected to direct sunlight for 2–3 h to conduct photolytic deterioration in the sunlight. This tablet powder was delivered to a 100 ml volumetric cup and could produce the prescribed amount of the mobile phase after pressure has been set. The solution's

Figure 3 RP-HPLC chromatogram of acid degeneration



spectra are next examined. The partial disintegration of the LRD molecule and unregulated interaction with medicinal additions result from this breakdown process, as seen in Figure 6, where even the HPLC-UV peaks seem uneven and occasionally overlapped.

4.4.5 Thermal degeneration. Powder mixture containing 60 mg of LRD tablet powder was stored on a glassware Petri dish and cooked in a hot air oven for 2 to 3 h at 105˚C. After a certain period, the tablet powder was weighed and then stirred in a milliliter of the volumetric flask to the point at which the staining of the moveable part had occurred. Maintaining the synthetic design of the LRD and consequently producing temperature-dependent dissolution of the chemicals at temperatures above 100˚C is difficult; the image can be seen in Figure 7.

4.5 Infrared spectrophotometer of LRD (Ebrahimzdeh *et al., 2013*; Mozameh and Mozahammadr, *2015*; Pavalache *et al., 2016*; Ganescu *et al., 2014*; Al-Salman *et al., 2020c*)

At Basra University/College of Education for Pure Sciences, the IR spectrum for influence the achievement potassium bromide is contained inside disc KBr was obtained using a

Figure 4 RP-HPLC chromatogram of Base degeneration

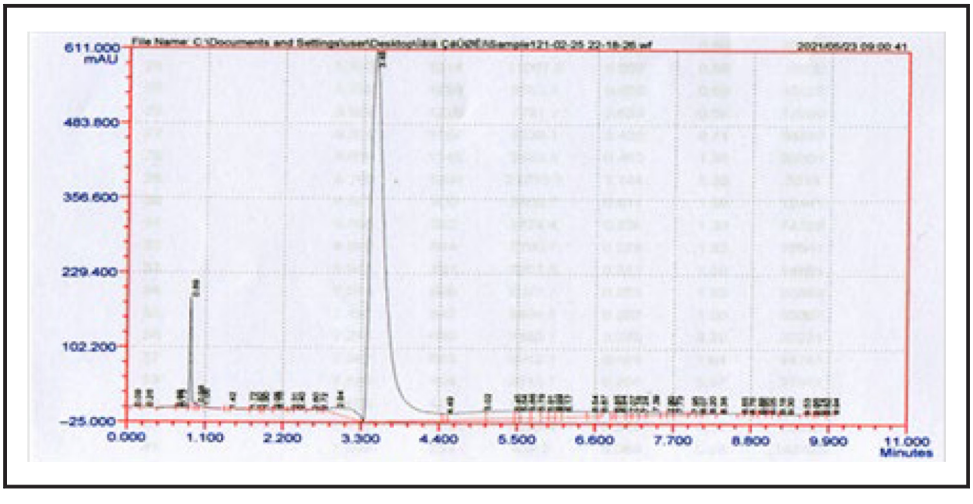
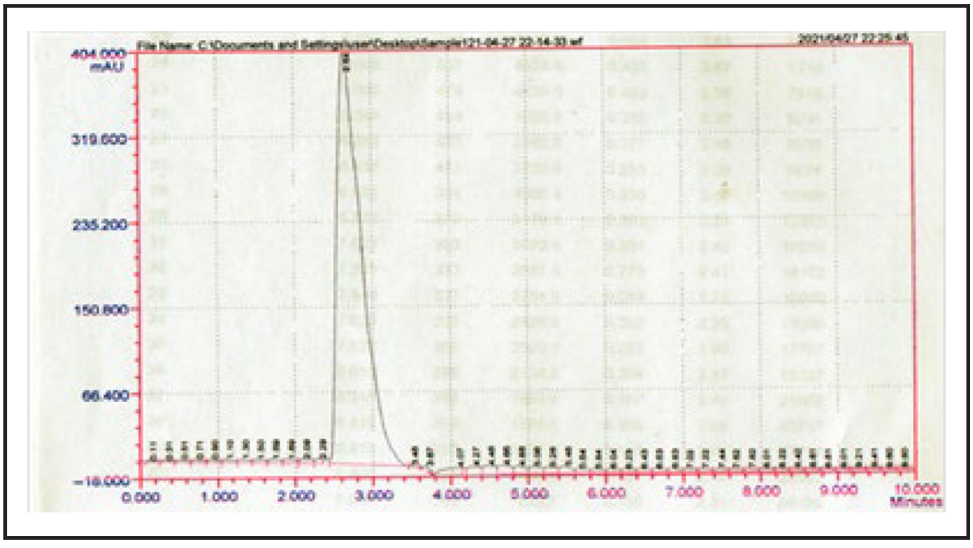


Figure 5 RP-HPLC chromatogram of oxidative degradation



machine of the type FTIR-84005-SHIMADZU, Origin of product Germany in the region (4,000,500 cm^{-1}) at room temperature. The FT-IR spectra of the compound LRD, which displays the organized components, are shown in Table 2.

4.5.1 For LRD – standard. LRD –standard's infrared spectrum (Figure 8, Table 2) reveals significant peaks for asymmetric stretching oscillations, which are consistent with its composition. The FT-IR spectra of standard–LRD appears feeble, with lines at 3,415 cm^{-1} (M) for (OH) Carboxylic acids and 1,604 cm^{-1} (S) for (C = O) Carboxylic acids, 1,730 cm^{-1}(S) for (C = O) Keton, 1,205 cm^{-1}(M) and 759 cm^{-1}(M) for (C-N), 1,467 cm^{-1} (M) for (C = N), 3,415 cm-1(m) for Aromatic C = C peaks emerge in the range 1,411 cm^{-1} (M).

4.5.2 For LRD – sample. The LRD graph's infrared spectrum (Figure 9, Table 2) exhibits peaks that match to the conventional model's peaks, with vibrations that display extensions and curvature conforming to its construction. The FT-IR spectra of standard-LRD tended to

Figure 6 RP-HPLC chromatogram of photolytic degeneration

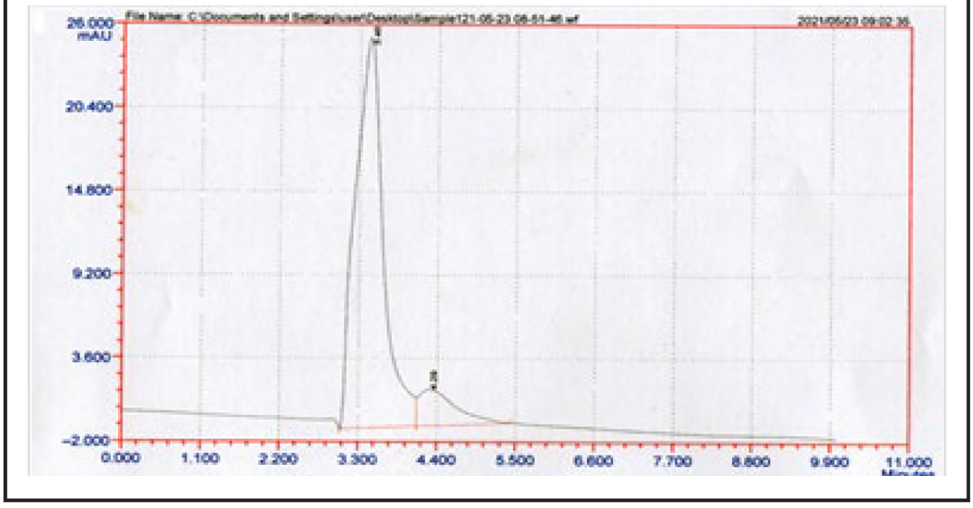


Figure 7 RP-HPLC chromatogram of thermal degeneration

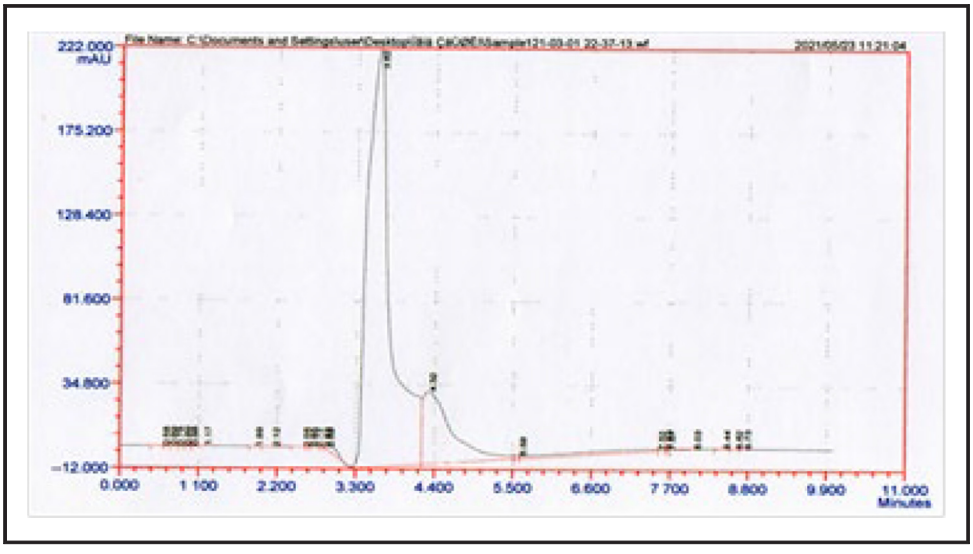


Table 2 LRD has distinct absorption bands in the infrared spectrum

Functional groups	*LRD-sample(cm^{-1})*	*LRD -Standard (cm^{-1})*
1 (OH) Carboxylic acids	3,460 m	3,415 m
2 (C = O) Carboxylic acids	1,604 S	1,604 S
3 (C = O) Keton	1,732 S	1,730 S
4 (C-N)	1,205 m	1,205 m
	759 m	759 m
5 (C = N)	1,471 m	1,467 m
6 (N -H)	3,419 m	3,415 m
7 (C-H) aromatic	3,059 w	3,062 w
8 (C-H) aliphatic	2,962 m	2,962 m
9 (C = C) aromatic	1,409 m	1,411 m

Figure 8 FT-IR spectrum of LDR standard

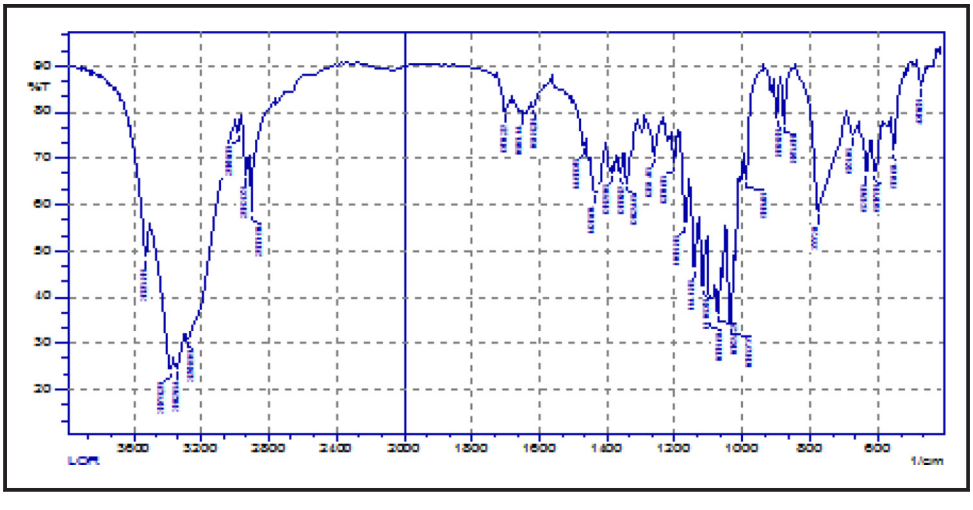
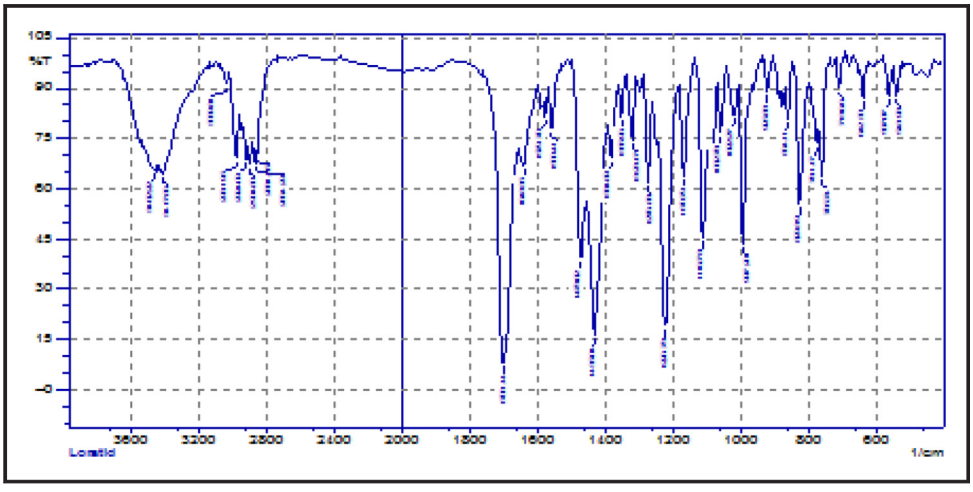


Figure 9 FT-IR spectrum of LDR – Sample



lose, with peaks at 3,460 cm^{-1} (M) for (OH) carboxylic acids and 1,604 cm^{-1} (S) for (C = O) carboxylic acids, 1,732 cm^{-1}(S) for (C = O) Keton, 1,205 cm^{-1}(m) and 759 cm^{-1}(M) for (CN), 1,471 cm^{-1} (M) for (C = N), 3,419 cm^{-1}(m) for (N- Aromatic C = C peaks exist in the range 1,409 cm^{-1} (M).

Notes: S = strong, M = middle, W = weak.

5. Discussion of the results

5.1 Importance of optimal HPLC conditions

(#27) The chromatographic parameters were chosen to extract all of the LRD peaks' byproducts. During the HPLC methodology optimization process, numerous experiments were conducted using the Ion Pac Arcus EP-C18; 5 m, 4.5 mm, 250 mm, with the suitable organic phase, Methanol: Acetonatrile (60:40) v/v. dibasic potassium phosphate buffer, at pH 7.2 and 1 ml/min flow rate. The wavelength was discovered to be 340 nm. LRD had a concentration of 3.3–3.8 min. The novel analytical method produced a good characterized by a high, as seen in (Figure 10).

5.2 System suitability

The HPLC-UV system was subjected to research to adapt it. Three copies of the same concentration were duplicated using the ideal approach using the regular LRD (3 g/mL). The system applicability is shown in Table 3. These successfully penetrated the separating theory's standards as well as LRD estimations in a variety of medicines (Abd-Alrassol *et al.*, 2020).

5.3 Validation of method and assay

The new chromatography technique HPLC-UV and criteria, such as selectivity, linearity spectrum, sensitivities, precision, regression and stiffness, were used to evaluate the technique in compliance with ICH guidelines (ICH, 1996). The effect of experimental circumstances on the peak regions of the analytes was examined to determine technique validity. The technique's validity is assessed at a concentration of 3 g/ml for LRD. All the findings were summarized in Table 4. The results showed that a bit of change in rotation

Figure 10 RP-HPLC obtained chromatogram after method of optimization

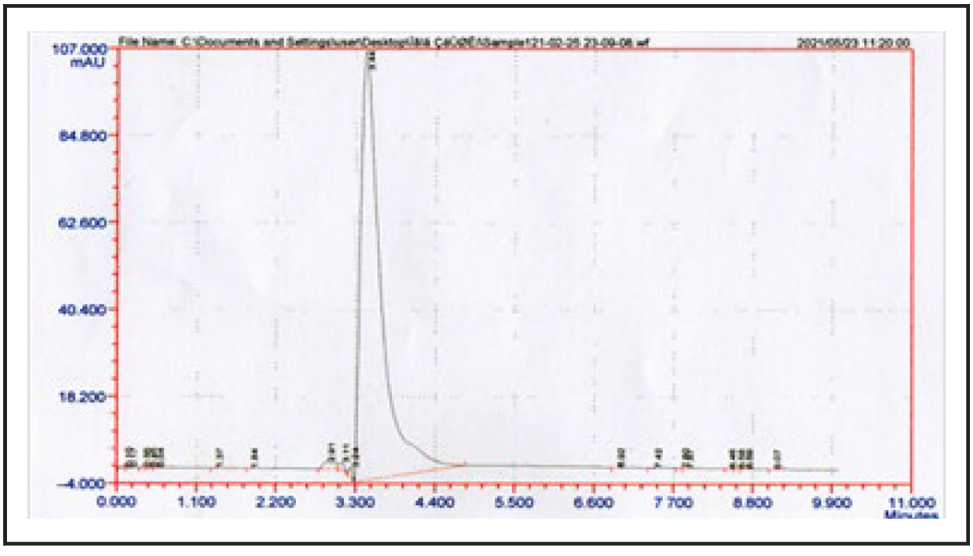


Table 3 System suitability

Parameters	*Value of LRD*	*Recommended limits*
Resolution	3.3–3.8 min	≥5
Peak area	214671.3 (%RSD 0.137)	RSD≤ 1
Retention time	3.38 (%RSD 0.147)	RSD≈ 0.101
USP tailing factor	5.184	≤1.9 – 2.5
Retention time	3.38 (%RSD 0.147)	RSD≈ 0.101

speed, the artwork of the mobile phase, temperatures and detecting wavelength had no effect on the peak regions for the medications, demonstrating that the approach was valid.

5.4 Specificity

Forced restriction was used to investigate the specificity of the proposed scheme. The investigation was carried out to ensure that the suggested approach could distinguish LRD from the probable degrading products manufactured during the forced degradation investigation. Acid, base, oxidation, photolysis and heat were used to study the tablet sample at a concentration of 3 g/ml LRD. The outcomes of forced disintegration are shown in Table 5. Figures 3–7 depict the shapes of chromatograms. The drug's alkaline conditions led to the highest proportion of degradation (Al-Salman *et al.*, 2018a). In the event of heat and photosynthetic deterioration, the lowest percentage of LRD degradation occurred. Decomposition products showed a single peak of deterioration. Other stress-related

Table 4 Measurement results for test method robustness

Parameter	*DPH (3 μg/ml)*		
	Found (μg/ml)	*%Recovery*	*%RSD*
System	6.0	100.0	0.192
Analyst	6.0	100.0	0.101

Table 5 Results of forced degradation studies

Type of degradation	*LRD (60 μg/ml)*	
	%Recovery	*%Degradation*
Photolytic	90.102	1.154
Acid	98.323	1.241
Undegraded	100	1.1880
Oxidative	92.944	2.942
Base	96.021	1.052
Thermal	95.541	1.140

chemical compounds do not interfere with the observation of LRD. Hence, the approach can be used as a reliability monitor.

5.5 Linearity range and sensitivity

By graphing the pinnacle areas for the drug against both the medication fixation (g/ml) under optimum test settings, a direct link was established. For LRD, the focus region was discovered to be (1–5) g/ml. The following requirements were obtained from the direct relapse study of the data:

$$y = 21959x \ (R^2 = 0.9998) \text{ for LRD}$$

On the basis of the following assumptions: y = peak area, x = drug convergence (g/mL), and *R*2 = regression coefficient (Al-Salman and Qanber, 2018b),. The high relapse coefficient predictions with a small catch reflect the modification bend's outstanding linearity, as shown in Figure 11.

5.6 Regression

Measuring the limits of quantitation (LLOQ) and border of detecting helped analyze the suggested process's comprehension (LLOD). The following equations were used to estimate the LOD and LLOQ (Al-Salman, 2017):

$$LLOQ = 10 \times SD/S; \ LLOD = 3.3 \times SD/S$$

Figure 11 Linearity of the calibration curve

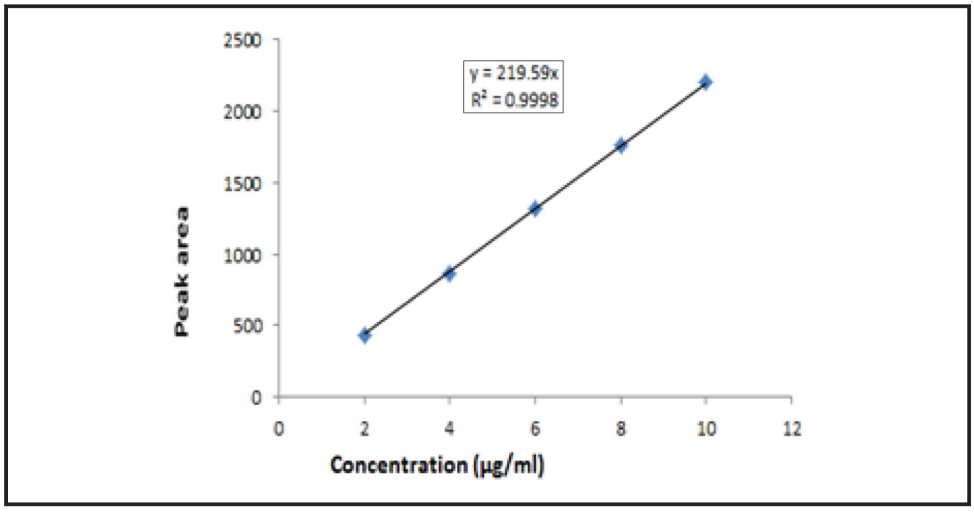


Table 6 Regression data of the proposed scheme

R^2	0.9998
LLOQ (μg/ml)	2.15
Standard error estimate	~ 0.00
LLOD (μg/ml)	0.92
Slope	21959
Intercept	~0.00
Standard error	~0.00

Wherever, SD denotes the pharmaceutical rejoinder's confidence interval and S denotes the calibration curve's slope. LLOQ values were determined to be 0.85 g/ml, whereas LLOD values were discovered to be 0.33 g/ml. These figures demonstrate that the anticipated technology's sensitivity for the evaluation of the chosen medication is adequate. The regression statistics of the predicted procedure are shown in Table 6 (AL-Sowdani and Al-Salman, 2016).

5.7 Accuracy

A measured quantity of standards mixture was taken to the pre-analysis tablet test solution at three different levels, 10%, 20% and 30%. The projected approach was used to re-analyze the results. With a percentage of RSD of 0.3%, the percent composition was between 96% and 100%. The results show that the technique is very accurate. The noninterference of the excipients was determined by analyzing the analyses to determine the process's selectivity (Alkamil *et al.*, 2020). Table 7 shows a summary of the findings.

5.8 Precision

LRD was analyzed at a concentration of 3 g/ml to define precision. There is some validity to the method was done by applying the established approach for estimating LRD in pure standard LRD three times (n = 3). The method's precision was tested by repeating the LRD inquiry in tablet samples three times (n = 3). Table 8 shows a summary of the findings. The percentages RSD values for system precision and methodology precision were both less than 0.3%, indicating that the proposed technique has a high degree of precision in regards to study of LRD (Alsaad *et al.*, 2019).

5.9 Applications of method

Examining commercially available tablets (LRD-Lincoln-LPL®, India, tablets containing various amounts from standard LRD −5 mg tablets) was used to analyze the analytical procedure of LRD-5 mg. The proportion of Standard- LRD was discovered to be 100 0.216%, whereas the ratio of LRD-5 (Lincoln-LPL®, India) was discovered to be 99 0.212%. This result indicates the proposed method was accurate and exact in LRD analysis in active

Table 7 Summarized results of accuracy

Claimed conc. ($\mu g\ ml^{-1}$)	*Found conc.* ($\mu g\ ml^{-1}$)	*Recovery* ±*RSD*
2	2.0	100 ± 0.102
4	4	100 ± 0.144
6	5.9	98.3 ± 0.101
6.0 μg ml^{-1} for drugs (LRD - Lincoln-LPL®, India-5mg)	6.0	100 ± 0.192

Table 8 Results of precision studies

Claimed conc. ($\mu g\ ml^{-1}$)	*Intraday*		*Interday*	
	Found ($\mu g\ ml^{-1}$)	*Recovery ± RSD%*	*Found (μg/ml)*	*Recovery ± RSD%*
2	2	100 ± 0.102	2	100 ± 0.122
4	4	100 ± 0.144	4.1	102 ± 0.108
6	5.9	98.3 ± 0.101	5.8	96.6 ± 0.101
8	7.9	98.75 ± 0.171	8.0	100 ± 0.144
10	9.8	98 ± 0.155	9.8	98 ± 0.110
6.0 μg/ml drug (LRD - Lincoln-LPL®, India-5mg)	6.0	100 ± 0.192	6.0	100 ± 0.189

Table 9 Assay of LRD in tablets

Analyte	*Labeled claim (mg)*	*Found (mg)*	*Mean (mg)*	*%Recovery*	*%RSD*
Standard - LRD	5	5	5	100	±0.101
LRD - Lincoln-LPL®, India-5mg	5	4.9	4.89	98	±0.192

ingredients, as indicated by the per cent recovery and RSD percent values. The outcomes of the applicants were reported in Table 9.

6. Conclusion

This study used a UV detector and an HPLC system (LC100 Angstrom advanced) to determine LRD in two new medicinal medicines. This created approach is simple, inexpensive and only requires a minimal amount of material. This system is the specific result of a single peak in the chromatogram provided by an ultraviolet detector. Because the prescription medications have such a low concentration, high sensitivity is not required in this usage. The solution was prepared according to HPLC-UV criteria, and the developed methodology meets Beer's law for pharmaceutical fixation in the range of 2–10 g/mL.

This research reveals the crucial analysis model used to determine the presence of LRD in the data structure based on the findings. The FDA's LRD measurement method is accurate, accurate, sensitive, precise, harsh and hearty. In this way, the suggested approach can be used to test LRD in tablet dose structures regularly.

References

Abd-Alrassol, K.S., Al-Salman, H.N.K., Jasim, E.Q. and Hussein, H.H. (2020), "Determination and evaluation of doses of metronidazole in different quantities and formulations with multiple spectroscopic methods", *Sys Rev Pharm*, Vol. 11, pp. 130-139.

Abu-Rumman, A. (2021), "Transformational leadership and human capital within the disruptive business environment of academia", *World Journal on Educational Technology: Current Issues*, Vol. 13 No. 2, pp. 178-187, doi: 10.18844/wjet.v13i2.5652.

Abu-Rumman, A., Al Shraah, A., Al-Madi, F. and Alfalah, T. (2021), "Entrepreneurial networks, entrepreneurial orientation, and performance of small and medium enterprises: are dynamic capabilities the missing link?", *Journal of Innovation and Entrepreneurship*, Vol. 10 No. 1, p. 29, doi: 10.1186/s13731-021-00170-8.

Alkamil, R.D.S., Al-Bahadily, D.C.H., Chaloob, R., Shari, F.H. and Al-Salman, H.N.K. (2020), "Estimation of truffles extracts and study the biological efficacy of ethyl 6-methyl-2-oxo-4-(2-thienyl)-1,2,3,4-

tetrahydropyrimidine-5-carboxylate (EMOTTC) as one of the extracts against ophthalmic bacteria", *Sys Rev Pharm*, Vol. 11, pp. 878-887.

Alsaad, A.A.A., Alassadi, E.A.S., Al-Salman, H.N.K. and Hussein, H.H. (2019), "The simultaneous determination of ibuprofen and paracetamol in pharmaceutical formulations by high performance liquid chromatography with ultraviolet detection", *Asian Journal of Pharmaceutics*, Vol. 13, p. 141.

Al-Salman, H.N.K., Alassadi, E.A.S., Fayadh, R.H., Hussein, H.H. and Jasim, E.Q. (2020a), "Development of the stable, reliable, fast and simple RP-HPLC analytical method for quantifying Diphenhydramine-Hcl (DPH) in pharmaceuticals", *International Journal of Pharmaceutical Research*, Vol. 12, pp. 4457-4467.

Al-Salman, H.N., Ali, E.T., Almukhtar, O.A. and Jabir, M.S. (2020b), "2-benzhydrylsulfinyl-N-hydroxyacetamide extracted from fig: a good therapeutic agent against Staphylococcus Aureus", AIP Conference Proceedings 2213-020223

Al-Salman, H.N.K., Ali, E.T., Jabir, M., Sulaiman, G.M. and Al-Jadaan, S.A.S. (2020c), "2-Benzhydrylsulfinyl-N-hydroxyacetamide-Na extracted from fig as a novel cytotoxic and apoptosis inducer in SKOV-3 and AMJ-13 cell lines via P53 and caspase-8 pathway", *European Food Research and Technology*, Vol. 246 No. 8, pp. 1591-1608.

Al-Salman, H.N.K., Hussein, H.H. and Maan, A.N. (2018a), "Quantitative analysis of cephradine using the modern high-performance liquid chromatographic method", *Asian J. Pharm*, Vol. 12, pp. 228-234.

Al-Salman, H.N.K. and Qanber, J.E. (2018b), "Analytical methods for diagnosis a mixture of narcotic substances in seized materials", *Int J. Green Pharm*, Vol. 12, pp. 216-226.

Al-Salman, H.N.K. (2017), "Analysis methods and qualitative diagnosis chromatographic for mixture of narcotic substances in seized materials", *Eur J. Sci Res*, Vol. 147, pp. 403-411.

Al-Sowdani, K.H. and Al-Salman, H.N.K. (2016), "Semi-automatedhome-made HPLC-UV system for determination ofamoxicillin trihydrate (AMO) in antibiotic drugs", *J Chem Biol Phys Sci*, Vol. 6, pp. 31-38.

Bîrsan, M., Cojocaru, I.C., Scutariu, M.M. and Popovici, I. (2014), "Validation of a chromatographic method for miconazole assay from oral sustained release mucoadhesive tablets", *Farmacia*, Vol. 62 No. 3, pp. 555-563.

Council of Europe (2013), *European Pharmacopoeia*, 8th ed., Council of Europe, Strasbourg.

Ebrahimzdeh, H. Molaei, K. Asgharinezhad, A.A. Shekari, N. and Dehghani, Z. (2013), "Analytica chimica acta, 767", p. 155.

Fayadh, R.H., ALSalman, H.N.K. and Hussein, H.H. (2021), "A quick, simple, and specific stability indicating RP-HPLC technique for determining valsartan in pharmaceuticals was developed and the validated", *Annals of the Romanian Society for Cell Biology*, Vol. 25 No. 4, pp. 16553-16570, ISSN:1583-6258.

Ganescu, A. Maureseanu, M. Ionescu, E. and Popescu, M. (2014), "Rev. Chim. (bucharest), 65, 5", p. 512.

Hasan, H.S., Abdallah, A.A., Khan, I., Alosman, H.S., Kolemen, A. and Alhayani, B. (2021), "Novel unilateral dental expander appliance (udex): a compound innovative materials", *Computers, Materials & Continua*, Vol. 68 No. 3, pp. 3499-3511, doi: 10.32604/cmc.2021.015968.

Hydrotropicsolubilisation Phenomenon (2015), "Hydrotropicsolubilisation phenomenon", *Journal of Drug Discovery and Therapeutics*, Vol. 3 No. 27, pp. 08-10.

ICH Harmonized-Tripartite Guidelines (2005), Validation of Analytical Procedure: Text and Methodology Q2 (R1), November.

ICH (1996), "Q2B, harmonized triplicate guideline, validation of analytical procedure methodology", *Proceeding of the International Conference on Harmonization*, IFPMA, Geneva.

Khan, I.U., Ashfaq, M., Razzaq, S.N. and Mariam, I. (2013), "Simultaneous determination of piroxicam and paracetamol in pharmaceutical formulations using stability indicating HPLC method", *Journal of Liquid Chromatography & Related Technologies*, Vol. 36 No. 10, pp. 1437-1450.

Kwekha-Rashid, A.S., Abduljabbar, H.N. and Alhayani, B. (2021), "Coronavirus disease (COVID-19) cases analysis using machine-learning applications", *Applied Nanoscience* , doi: 10.1007/s13204-021-01868.

Mozameh, P. and Mozahammadr, H. (2015), "Journal of chromatography B, 980", p. 41.

Palade, L., Popovici, I., Popa, G. and Cojocaru, I. (2013), "Elaboration and validation of an HPLC method for the quantitative assay of 5-Fluorouracil", *Farmacia*, Vol. 61 No. 3, pp. 526-532.

Pani, N.R., Acharya, S. and Patra, S. (2014), "Development and validation of RP-HPLC methodfor quantification of glipizide in biological macromolecules", *International Journal of Biological Macromolecules*, Vol. 65, pp. 65-71, Apr.

Pavalache, G. Dorneanu, V. and Popescu, A. (2010), "Ovidius university annals of chemistry, 21", p. 157.

Pavalache, G. (2011), "Validation of an analytical method based on highperformance liquid chromatography for determination of loratadine inpharmaceutical preparations and biological environments", *Farmacia*, Vol. 59 No. 2, pp. 201-208.

Pavalache, G. Dorneanu, V. and Popescu, A. (2010), "Acta medica transilvanica, 2, nr. 4", p. 276.

Pavalache, G. Dorneanu, V. and Popescu, A. (2016), "Chim. (bucharest), 67, 1", p. 30.

Ponnilavarasan, I. (2011), "Simultaneous estimation of ambroxol hydrochlorideand loratadine in tablet dosage form by using uv spectrophotometric method", *International Journal of Pharma and Bio Sciences*, Vol. 2 No. 2, pp. 338-344.

Ramulu, G., Ravindra Kumar, Y., Vyas, K., Suryanarayana, M.V. and Mukkanti, K. (2011), "A new validated liquid chromatographic method for the determination of loratadine and its impurities", *ScientiaPharmaceutica*, Vol. 79, pp. 277-291.

Shalini, K.B. and Sahoo, N.K. (2014), "Development and validation of loratadine in bulk and pharmaceutical dosage form by uv spectroscopic method", *International Journal of Pharmaceutical Research & Analysis*, Vol. 4 No. 1, pp. 39-43.

Sujatha, T. and Balmuralikrishna, K. (2014), "RP-HPLC method for the estimation of loratadine [LRD] in bulk drug and in tablet dosage forms", *Der Pharmacia Sinica*, Vol. 5 No. 2, pp. 39-44.

Sujatha, T. Alikrishna, K. and Ramesh Raju, R. (2014), "Der pharmacia sinica, 5, 2", p. 39.

United States of Pharmacopoeia (2007), *30/National Formulary-25*, Asian ed., UnitedStates Pharmacopoeial Convention, Inc., Rockville, MD, Vol. 2, p. 2492.

Walash, M.I., Belal, F., el-Enany, N., Eid, M. and el-Shaheny, R.N. (2011), "Stability-indicating micelle-enhanced spectrofluorimetric method for determination of loratadine and desloratadine in dosage forms", *Luminescence*, Vol. 26 No. 6, p. 670.

Youssef, R.M., Khamis, E.F., El-Sayed, M.A. and Abdel Moneim, M.M. (2012), "Journal of planar chromatography 25, 5", p. 456.

Further reading

Alassadi, E.A.S., Jasim, E.Q., Al-Salman, H.N.K. and Mosa, M.N. (2020), "Comparative study of an in vitro release patterns of ceftaroline fosamil fom chemically – prepared coated hydroxyapatite nanoparticles", *Sys Rev Pharm*, Vol. 11, pp. 797-805.

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