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ESTIMATION AND VALIDATION OF QUINIODOCHLOR BY HYDROTROPIC SOLUBILIZATION METHOD

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ABSTRACT

Various organic solvents such as methanol, chloroform, dimethylformamide and acetonitrile have been employed for solubilization of poorly water-soluble drugs to carryout spectroscopic analysis. Drawbacks of organic solvents include their higher cost, toxicity and pollution. Hydrotropic solubilization may be a proper choice to preclude the use of organic solvents. It involves the addition of large amount of second solute to increase the aqueous solubility of first solute. These hydrotropes are economic and pollution-free. In the present investigation, 40% urea solution was employed as hydrotropic solubilizing agent to solubilize poorly water-soluble drug Quiniodochlor. Quiniodochlor exhibits absorption maximum at 267nm. In this method, no interference from any additives and diluents in the estimation of drug was seen. Beer's law was found to be obeyed in concentration range of 5-25µg/ml. The results of analysis have been validated as per ICH guidelines. The method is accurate, precise and economical.

KEYWORDS: Hydrotropic solubilization, Quinidiochlor, Uv spectroscopy.

INTRODUCTION

A solute's aqueous solubility can be increased by adding a significant amount of second solvent, a process known as hydrotropy. Alkali metal salts of different organic acids make up the solute. Ionic organic salts are indicated as hydrotropic agents. The term "salt in" refers to an additive or salt that makes a solute more soluble in a particular solvent, whereas the term "salt out" refers to a salt that makes the solute less soluble. Some salts that have big anions or cations and are highly soluble in water cause non-electrolytes to "salt in," a phenomenon known as "hydrotropism.". Hydrotropic solutions have a weak interaction between the

hydrotropic agent and the solute and do not exhibit colloidal properties. When a lot of additives are present, their solubility in water increases—a phenomenon known as hydrotropy. The process by which it increases solubility is more closely associated with a complexation in which the poorly soluble drugs and hydrotropic agents such as sodium benzoate, sodium acetate, sodium alginate, and urea interact weakly. A hydrotropic substance must have good water solubility, which is produced by the anionic group. On the other hand, the hydrophobic portion plays a crucial role in the hydrotropic solubilization process. A polar group carries the hydrophobic planar structure of hydrotropic agents into solution. As a result, compounds having a polar group and a hydrophobic planar component behave like hydrotropic agents and are not intrinsically anionic. Advantages of hydrotropic solubility include; Environmentally friendly approach for analyzing poorly water-soluble pharmaceuticals, No toxicity, Simple method, Economical method and It does not modify hydrophobic medicines chemically.

Quiniodochloris a drug that is antifungal and anti-protozoal. It belongs to a class of medications known as hydroxyquinolines, which block some enzymes involved in DNA replication. Due to their low cost, these medications were indiscriminately and widely used for the prevention and treatment of traveler's diarrhea, nonspecific diarrhea, and dietary errors. Eighth-hydroxyquinolines have few negative effects, such as nausea, momentary loose and green stools, itching, etc., but if taken incorrectly, they can be toxic. With prolonged consumption, goiter and lodism (furunculosis, an inflammation of the mucous membranes) may occur. Iodine sensitivity can cause an acute reaction in some people, including fever, chills, angioedema, and cutaneous bleeding.

The goal of this study is to develop a new, simple, safe, environmentally friendly, economic, costeffective and accurate method for the estimation and validation of quinidiochlor tablet.

MATERIALS AND METHOD

Preliminary solubility study (Selection of hydrotropic agent)

In the solubility study, it was found that there was more than six fold enhancement in the solubility of Quiniodochlor in 40% urea hydrotropic solution at room temperature.

Estimation of Quiniodochlor by UV Spectroscopy

Preparation of standard stock solutions

100mg of Quiniodochlor was weighed accurately and transferred to a beaker; to this 70 ml of

40% urea solution were added. Mechanically stirred for 6hours. Makeup the volume to 100ml with 40% urea solution. Standard stock solution of concentration1000µg/ml is obtained. The stock solution was diluted with distilled water to obtain different concentrations in the range 5-25µg/ml. calibration curve plotted by noting absorbance at 200-300nmagainst corresponding blank. The wavelength at which Quiniodochor showed maximum absorbance was found to be 267nm (Figure 1)

Preparation of test solution

Tablet powder equivalent to 100 mg was weighed accurately and added to 70 ml 40% urea solution. Mechanically stirred for about 6 hours. Make up the volume to 100ml with 40% urea solution. Test solution of concentration 1000µg/ml is obtained. The solution was diluted with distilled water to obtain different concentrations in the range 5-25µg/ml. calibration curve plotted by noting absorbance at 200-300nmagainst corresponding blank. The wavelength at which Quiniodochor showed maximum absorbance was found to be 267nm (figure 2).

To study accuracy precision and reproducibility of proposed method recovery studies were conducted by spiking the preanalysed tablet with pure drug at two Levels and Following the same proposed analysis method.

Validation of method

- **Linearity and Range:** The aliquots of concentration ranging from 5-50µg/ml were prepared in triplicate, but linearity was found to be between 5-25µg/ml concentrations. At a wavelength of 267 nm, the solutions were examined, and absorbance were recorded. By graphing the absorbance v/s concentration of Quiniodochlor, a calibration curve was created. Quiniodochlor's least square linear regression correlation coefficient (r2) was computed. (table 1)
- **Precision:** The reproducibility and intermediate precision (intraday precision) of the analytical procedure were examined. On three consecutive days, the method's intermediate precision was assessed using the same procedure by calculating there actions of the working standard solution three times, repeatability experiments were conducted. The findings were presented as percentage relative standard deviation (%RSD) of the total results. (Table 2&3)

RESULTS AND DISCUSION

The aim of the study was to perform and validate a simple, economic, precise, and reproducible UV spectrophotometric method for a poorly water-soluble drug Quiniodochlor by improving its hydrotropic solubility. The literature review was done to gather information about the hydrotropic solubility technique and UV spectrometric method development and validation. The solubility of Quiniodochlor in various hydrotropic agents like sodium benzoate and urea was examined during preliminary solubility study. The 40% urea solution has increased the solubility of Quiniodochlor by 6 fold and was selected as an hydrotropic agent for our study. The standard and test solution soft hedrugwere prepared. The stock solutionswerefurther diluted using distilled water to get concentrations 5-25ug/ml. Then standard and stock solutions were scanned under from 200-300nm. Then the linearity of test sample was examined and the correlation coefficient was found to be less than 1, so the method was linear. Then the accuracy of the method was examined by using standard addition method and percentage recovery was calculated. The relative standard deviation found to be less than 2, So the method was accurate. The precision of the method was validated in both intermediated and repeatability conditions. The test results were found to be within the acceptance criteria. The LOD and LOQ of the method were determined using Standard Deviation of the Blank (SDB). The robustness was determined by checking the absorbance at two selected wavelength 265nm and 269nm.

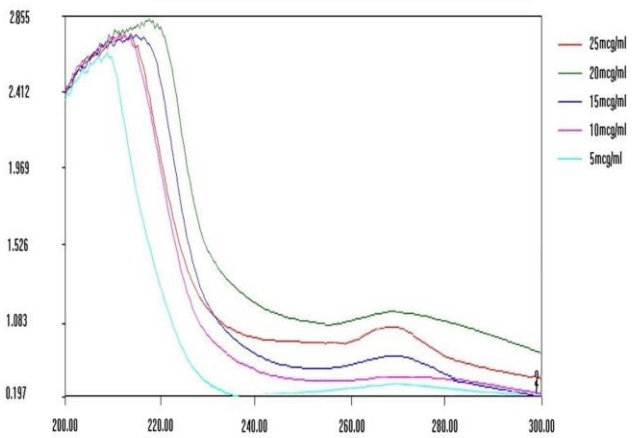

Figure 1: Absorption spectrum of standard quiniodochlor.

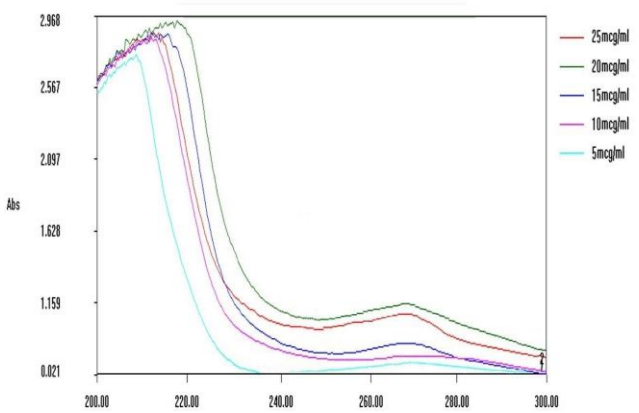

Figure 2: Absorption spectrum of quiniodochlor table.

Table 1: Accuracy result of quiniodochlor tablet.

Reps	Conc (%)	Conc. of sample (µg/ml)	Conc. of std. added(µg/ml)	Absorbance (nm)	% Recovery	Mean% recovery	% RSD
1	80	10	8	0.873	98.13	97.99	0.45
2		10	8	0.870	97.49		
3		10	8	0.874	98.35		
1	100	10	10	0.985	97.68	97.92	0.53
2		10	10	0.983	97.34		
3		10	10	0.989	98.37		
1	120	10	12	1.095	97.10	97.19	0.16

Table 2: Intraday precision (Repeatability) results of quiniodochlor.

Time (hrs)	Concentrationof sample(mcg/ml)	Absorbance (nm)
0	10	0.414
1	10	0.417
2	10	0.419
3	10	0.415
4	10	0.416
Avg		0.416
SD		0.001
%RSD		0.462

Table 3: Intermediate precision results of quiniodochlor.

Concentration (µg/ml)	Absorbance(nm)			Average	SD	%RSD
	Day1	Day2	Day3			
10	0.415	0.427	0.403	0.415	0.006	1.45
15	0.741	0.752	0.768	0.753	0.013	1.80
20	0.952	0.968	0.947	0.955	0.01	1.14

Table 4: Robustness results of quiniodochlor.

Max.wavelength(nm)	265	269
Absorbance	0.406	0.411
	0.404	0.413
	0.406	0.410
Avg	0.405	0.411
SD	0.0011	0.0015
%RSD	0.285	0.371
LOD: 2.0783µg/ml LOQ: 6.2979µg/ml		

Table 5: Summary of validation.

Parameters	Values
Absorbance maxima	267nm
Linearity range	5-25µg/ml
Standard regression equation	y=0.0584x-0.1695
y-Intercept	0.1695
Correlation coefficient(R^2)	0.9976
Slope	0.0584
Accuracy	%RSD of %recovery was<2
Precision	% RSD <2

CONCLUSION

Thus it may be concluded that, this proposed study presents a spectrophotometric evaluation of Quiniodochlor, exposing the advantages of using hydrotropic agent as regards to simplicity, lower cost, and better sensitivity and precluding the use of organic solvents. The method is simple, precise and accurate for the determination of Quiniodochlor, in bulk and tablet dosage form.(Table5)

REFERENCESS

1. Kuchekar AB, Gawade A, Boldhane S. Hydrotropic Solubilization: An Emerging Approach. J Drug Deliv Ther, 2021; 11(1-s): 200–6.
2. Choudhary AN, Nayal S. Areview: Hydrotropyasolubilityenhancing technique. Pharma Innovation J, 2019; 8(4): 1149-53.
3. Verma G, Mishra M. Development and optimization of UV-Vis spectroscopy-a review. World J. Pharm. Res, 2018; 19, 7(11): 1170-80.
4. Aadil MR.Hetvi P. Dalwadi M. Shah C, Upadhyay U. UV spectroscopy and its applications: a review. World Journal of Pharmacy and Pharmaceutical Sciences, 2021; 10(11): 454-469.
5. Sayed R, Mohamed AR, Hassan WS, Elmasry MS. Comparative study of novel green

UV- spectrophotometric platforms for simultaneous rapid analysis of flumethasone pivalate and clioquinol in their combined formulation. Drug Development and Industrial Pharmacy, 2021; 3, 47(6): 867-77.

6. Chhalotiya UK, Bhatt KK, Shah AD, Baldania SL, Patel MR. Quantification of clioquinol in bulk and pharmaceutical dosage forms by stability indicating LC method. Turk J Pharm Sci, 2014; 1, 11(1): 67-78.
7. Walfish S. Analytical methods: a statistical perspective on the ICH Q2A and Q2B guidelines for validation of analytical methods. BioPharm International, 2006; 1, 19(12): 1-6.
8. Breaux J, Jones K, Boulas P. Analytical methods development and validation. Pharm. Technol, 2003; 1: 6-13.
9. Patil CD, Matore BW, DhekalePS. Spectroscopic Determination Of Glipizide By Using Hydrotropic Solubilising Agent. International Journal of Current Advanced Research, 2017; 6(9): 5728-5730.
10. Veer SD, Dr. Bari SB, Patil DD, Shirasath NR. Novel method development and validation spectrometric analysisofq uetiapinef umaratetable tandbulkusingure aasahydrotr opicsolubilizer. International Research Journal of Modernization in Engineering Technology and Science, 2021; 3(5): 520-525.
11. Anekar VP, Mohite PM, Sankpal PS. Spectrop hotometri cmethodsforestima tionofartesu natefrom tablet dosage forms by hydrotrophy. Res J Pharmacol Pharmacodyn, 2020; 12(2): 88.
12. Kuchekar AB, Gawade A, Boldhane S. Hydrotropic Solubilization: An Emerging Approach. JDrug Deliv Ther, 2021; 11(1-s): 200–6.
13. ChoudharyAN, Nayal S. Areview: Hydrotropyasolubilityenhancing technique.Pharma Innovation J, 2019; 8(4): 1149-53.
14. Verma G, Mishra M. Development and optimization of UV-Vis spectroscopy-a review. World J. Pharm. Res, 2018; 19, 7(11): 1170-80.
15. Aadil MR.Hetvi P. Dalwadi M. Shah C, Upadhyay U. UV spectroscopy and its applications: a review. World Journal of Pharmacy and Pharmaceutical Sciences, 2021; 10(11): 454-469.
16. Sayed R, Mohamed AR, Hassan WS, Elmasry MS. Comparative study of novel green UV- spectrophotometric platforms for simultaneous rapid analysis of flumethasone pivalate and clioquinol in their combined formulation. Drug Development and Industrial Pharmacy, 2021; 3, 47(6): 867-77.

17. Chhalotiya UK, Bhatt KK, Shah AD, Baldania SL, Patel MR. Quantification of clioquinol in bulk and pharmaceutical dosage forms by stability indicating LC method. Turk J Pharm Sci, 2014; 1, 11(1): 67-78.
18. Walfish S. Analytical methods: a statistical perspective on the ICH Q2A and Q2B guidelines for validation of analytical methods. BioPharm International, 2006; 1, 19(12): 1-6.
19. Breaux J, Jones K, Boulas P. Analytical methods development and validation. Pharm. Technol, 2003; 1: 6-13.
20. Patil CD, Matore BW, Dhekale PS. Spectroscopic Determination of Glipizide By Using Hydrotropic Solubilising Agent. International Journal of Current Advanced Research. 2017; 6(9): 5728-5730.
21. Veer SD, Dr. Bari SB, Patil DD, Shirasath NR. Novel method development and validation spectrometri canalysiso fquetiapin efumaratetabletan dbulkusin gureaasahyd rotropic solubilizer. International Research Journal of Modernization in Engineering Technology and Science, 2021; 3(5): 520-525.
22. Anekar VP, Mohite PM, Sankpal PS. Spectrophot ometricmeth odsforestima tionofartes unatefrom tablet dosage forms by hydrotrophy. Res J Pharmacol Pharmacodyn, 2020; 12(2): 88.
23. Sharma MC, Sharma S. Spectrophotometric Determination and Application of Hydrotropic Solubilization in the Quantitative Analysis of Ranitidine Hydrochloride in Pharmaceutical Dosage Form. International Journal of PharmTech Research, 2011; 3(1): 253-255.
24. BernardS, Mathew M, Senthilkumar KL. Spectrophotometric methodofestimationof Amlodipine besylate using hydrotropic solubilization. Journal of Applied Pharmaceutical Science, 2011; 1(9): 177-180.
25. MaheshwariRK, SrivastavVK, Prajapat RP, Jain A, Kamaria P, Sahu S. New spectrophotometric estimation of ornidazole tablets employing urea as a hydrotropic solubilizing additive. Indian J Pharm Sci, 2010; 72(2): 258-261.
26. Sherje AP, Desai KJ. Spectrophotometric Determination of Poorly Water Soluble Drug Rosiglitazone Using Hydrotropic Solubilizationtechnique. Indian J. Pharm. Sci, 2011; 73(5): 579-582.
27. Maheshwari RK, Shukla RS. Quantitative Spectrophotometric Estimation of Famotidine Using Hydrotropic Solubilization Technique. Asian Journal of Chemistry, 2008; 20(6): 4221-4224.

28. Patel A, SoniML, ModiV, Jaliwala YA, Shukla R. Quantitative spectrophotometric estimation of cefadroxil using hydrotropic solubilization technique. Asian J Pharm, 2008; 2(3): 146-147.
29. Lee J, Lee SC, Acharya G, Chang CJ, Park K. Hydrotropic solubilization of paclitaxel: analysis of chemical structures for hydrotropic property. Pharmaceutical research, 2003; 20: 1022-30.
30. JainNK, PatelVV, Taneja LN. Hydrotropic solubilizationofnifedipine. Die Pharmazie, 1988; 1, 43(3): 194-6.
31. Mandour AA, Nabil N, Zaazaa HE, Abdelkawy M. Review on analytical studies of some pharmaceutical compounds containing heterocyclic rings: brinzolamide, timolol maleate, flumethasone pivalate, and clioquinol. Future Journal of PharmaceuticalSciences, 2020; 6: 1-0.
32. Akash MS, Rehman K, Akash MS, Rehman K. Ultraviolet-visible (UV-VIS) spectroscopy. Essentials of pharmaceutical analysis, 2020; 29-56.
33. Siddiqui MR, Alothman ZA, Rahman N. Analytical techniques in pharmaceutical analysis: A review. Arabian Journal of chemistry, 2017; 1, 10: S1409-21.
34. Dhapte V, Mehta P. Advances in hydrotropic solutions: An updated review. St. Petersburg Polytechnical University Journal: Physics and Mathematics, 2015; 1, 1(4): 424-35.
35. Patil MR, Ganorkar SB, Patil AS, Shirkhedkar AA, Surana SJ. Hydrotropic solubilization in pharmaceutical analysis: Origin, evolution, cumulative trend and precise applications. Critical reviews in analytical chemistry, 2021; 7, 51(3): 278-88.
36. Suzuki H, Sunada H. Mechanisti cstudieso nhydrotrop icsolubili zationofni fedipinein nicotinamide solution. Chemical and pharmaceutical bulletin, 1998; 15, 46(1): 125-30.
37. El-Houssieny BM, El-Dein EZ, El-Messiry HM. Enhancement of solubility of dexibuprofen applying mixed hydrotropic solubilization technique. Drug discoveries & therapeutics, 2014; 31, 8(4): 178-84.
38. Maheshwari RK, Rathore A, Agrawal A, Gupta MA. New spectrophotometric estimation of indomethacinc apsuleswithniaci namideashydr otropicsol ubilizingagent. Pharmaceut icalmethods, 2011; 1, 2(3): 184-8.
39. Jain N, Jain R, Thakur N, Gupta BP, Banweer J, Jain S. Novel spectrophotometric quantitative estimation oftorsemide in tablets using mixed hydrotropic agent. Der Pharmacia Lettre, 2010; 2, 2(3): 249-54.
40. Maheshwari RK, Wanare G, Chahar N, Joshi P, Nayak N. Quantitative estimation of

naproxen in tabletsusing ibuprofenso diumashydro tropicagent. Indianjour nalofpharm aceutical sciences, 2009; 71(3): 335.

41. Madan JR, Kamate VJ, DuaK, Awasthi R. Improvingt hesolubilit yofnevirapineus ingahydrotropy and mixed hydrotropy based solid dispersion approach. Polymers in Medicine, 2017; 47(2): 83-90.
42. Mishra AK, Kumar M, Mishra A, VermaA, Chattopadhyay P. Validated UV spectroscopicmethod for estimation of salbutamol from tablet formulations. Archives of Applied Science Research, 2010; 2(3): 207-11.
43. Gadhave NA, Ghante MR, Nikam AD, Sawant SD. Simultaneous estimation of tamsulosin hydrochloride and finasteride in combined dosage form by UV spectroscopy method. Journal of Pharmacy Research, 2011; 4(8): 2672-4.
44. Jani BR, Shah KV, Kapupara PP. Development and validation of UV spectroscopic method for simultaneous estimation of dapagliflozin and metformin hydrochloride in synthetic mixture. International Journal of Research and Development in Pharmacy & Life Sciences, 2015; 15, 4(3): 1569-76.
45. Wamorkar V, Manjunath S, Varma MM. Development andvalidation of UV spectroscopic method for determination of metoclopramide hydrochloride in bulk and tablet formulation. Int J Pharm Pharm Sci, 2011; 3(3): 171-4.
46. Gul S, Hameed A. UV spectroscopic method for determination of phenytoin in bulk and injection forms. Chem Int, 2018; 4(3): 177-82.
47. Upjohn AC, Galbraith HJ, Solomons B. Raisedserumprotein-bound iodineaftertopicalclioquinol. Postgraduate Medical Journal, 1971; 47(549): 515.
48. A. Sayed R, Mohamed AR, Hassan WS, Elmasry MS. Comparative study of novel green UV- spectrophotometric platforms for simultaneous rapid analysis of flumethasone pivalate and clioquinol in their combined formulation. Drug Development and Industrial Pharmacy, 2021; 3, 47(6): 867-77.
49. Khashaba P. Quantitation of tolnaftate by spectrophotometric methods in pharmaceutical formulations. Bulletin of Pharmaceutical Sciences. Assiut, 2002; 30, 25(1): 31-41.
50. Schaber PM, Hobika G. Determining the antifungal agent clioquinol by HPLC, the Not So Pure Preparation: a laboratory-based case study for an instrumentalan alyticalchemistrycourse. Journal of Chemical Education, 2018; 19, 95(3): 445-50.
51. Bhaskar O. Aher et al. Spectrophotometric Method Development and Validation of Poorly Water Soluble Drugby Using Urea as Hydrotropic Agent. Indo AmericanJournal of Pharmaceutical Research, 2016; 6(01).