Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 5, Issue, 02, pp.262-265, February, 2013

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

Comparative study on the Spectrophotometric determination of some selected 5-nitroimidazoles

***,[1]Pavan Kumar, G. V. S. R., [1]Sreeramamurty, B., [2]Sarma, N. V. L. N. and [2]Harsh Vardhan, T.**

[1,2]Department of Engineering Chemistry, M V G R College of Engineering Vizianagaram

ARTICLE INFO

Article History:
Received 18th November, 2012
Received in revised form
12th December, 2012
Accepted 21th January, 2013
Published online 14th February, 2013

Key words:
Spectrophotometry,
Nitroimidazoles,
5-nitroimidazoles,
Sulphanilamide,
NEDA

ABSTRACT

The present study is aimed at making a comparative study of the direct spectrophotometric determination of 5-nitroimidazoles such as metronidazole, ornidazole, tinidazole, secnidazole and satranidazole with 0.5% sulphanilamide and 0.3% NEDA. Each of the drug samples was boiled for 90 minutes at a temperature of 90°C followed by the treatment with the reagents 0.5% sulphanilamide and 0.3% NEDA. It exhibited a stable instantaneous reddish purple, colour, which showed maximum absorbance at 540nm. With each of the above mentioned drug samples, the same colour was observed and the maximum absorbance was at 540nm for all. Beer's law obedience, correlation factor, stability, LOD and LOQ were given below for a comparative study.

INTRODUCTION

Nitroimidazoles are synthetic antibacterial preparations with a high sensitivity against anaerobic microorganisms and protozoal infections. The first medication - metronidazole was approved for medical use in 1960. Another kind of nitroimidazoles include: tinidazole, ornidazole, secnidazole and ternidazole, a preparation for local application. Nitroimidazoles exhibit selective bactericidal action against those microorganisms in which enzymatic systems can reduce nitro group. Active reductive forms of medications inhibit DNA replication and protein synthesis in microbial cell and inhibit respiratory chains (cellular respiration). Nitroimidazoles are found to be active against the majority of gram-negative and gram-positive anaerobs and bacteroides (including B.fragilis), clostridium (including C. difficile), Fusobacterium spp., Eubacterium spp., Peptostreptococcus spp., P.niger, G.vaginalis. P.acnes are resistant to imidazoles. T.vaginalis, E.histolytica, G.lamblia, L.intestinalis, E.coli, Leishmania spp. are also resistant to nitroimidazoles.

These drugs are generally used in the treatment of Vaginitis, Bacterial vaginosis, Acne, Seborrheic eczema, Acne rosacea. The nitroimidazoles fall into different categories such as 2-nitroimidazoles, 4-nitroimidazoles[1] and 5-nitroimidazoles. 5-Nitroimidazole is an imidazole derivative which contains a nitro group. Several derivatives of nitroimidazole constitute the class of nitroimidazole antibiotics that have been used to combat anaerobic bacterial and parasiticinfections.[2] The most common example is metronidazole (Flagyl). Other heterocycles such as nitrothiazoles (thiazole) are also used for the same purpose. Nitroheterocycles may be reductively activated in hypoxic cells and then undergo redox recycling or decompose to toxic products.[3] Various 5-nitroimidazoles include metronidazole, ornidaole, secinidazole, tinidazole and satranidazole. For the quantitative determination of these drugs various methods such as spectrophotometric, electro-analytical, chromatographic and volumetric were found in literature [4-20]. In recent years a novel and direct visible spectrophotometric method for the determination of these drugs was developed and reported. The method was found to be accurate, simple, precise with a least LOD and LOQ over all the other methods so far found in the literature. It was found that all the five aforesaid drugs showed a stable, instantaneous reddish purple colored product by the reaction between the drug sample solution and the reagents 0.5% sulphanilamide and 0.3% NEDA. A complete ,critical comparative analysis report for the visible spectophotometric method developed in recent years was presented in Table.1.

Table 1. comparative analysis report

Drug sample / Parameter	Metronidazole	Ornidazole	Tinidazole	Secnidazole	Satranidazole
pH	3.5	3.5	3.5	3.5	3.5
Temperature	90	90	90	90	90
Beer's law obedience	200-600	100-300	100-600	100-500	50-300
Molar absorptivity	72.68	91.14	338.6	169.4	510.2
Stability	24	24	24	24	24
LOD	0.01	0.005	0.02	0.04	0.09
LOQ	0.04	0.015	0.7	0.13	0.3
Correlation coefficient	0.9978	0.9985	0.99994	0.9990	0.9994
λ maximum	540	540	540	540	540

Temperature in °C
Molar absorptivity is expressed in cm^{-1} lit $mole^{-1}$
Stability in hours
LOD and LOQ are expressed in μgmL^{-1}
λ maximum is expressed in nm
Beer's law obedience is expressed in μgmL^{-1}

Corresponding author: prs_ganti@yahoo.co.in

Effect of pH

It was found that the reaction between each of the drug sample solution 0.5% sulphanilamide and 0.3% NEDA is carried out at a pH 3.5. To achieve a pH 3.5, the reagent solutions 0.5% sulphanilamide and 0.3% NEDA were prepared using 20% (V/V) hydrochloric acid solution and 1% (V/V) hydrochloric acid solution respectively. It was found that each of the drug samples undergoes the reaction at the same pH value (Fig.1).

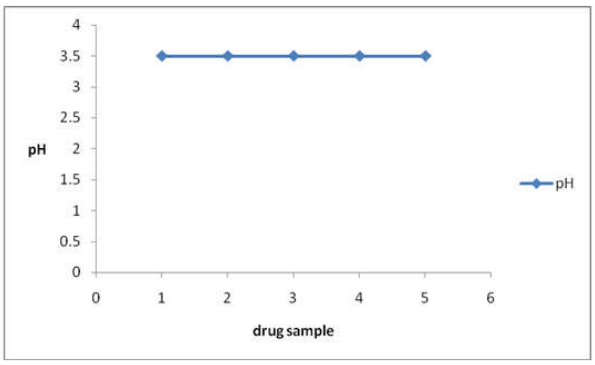

Fig. 1. Effect on pH on the reaction between the drug samples olution and specified reagents

Effect of temperature

During the preparation of drug sample solution, it was found that an adequate amount the powdered drug sample is weighed and dissolved in double distilled water and this solution is heated to a temperature of 90° C. Each of the above mentioned drug sample dissolved in double distilled water at the temperature of 90° C (Fig.2).

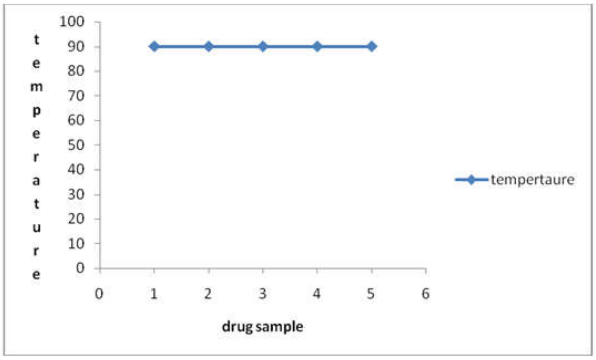

Fig. 2. Effect of temperature on the dissolution of the drug sample

Wavelength of maximum absorbance (λmax)

For each of the above mentioned drug sample analyzed, the stable instantaneous reddish purple colored product formed showed a maximum absorbance at 540nm. It was found that, though the drug samples vary in their physical and chemical properties, they responded to the specified reagents in the same manner in showing wave length of maximum absorbance (Fig.3).

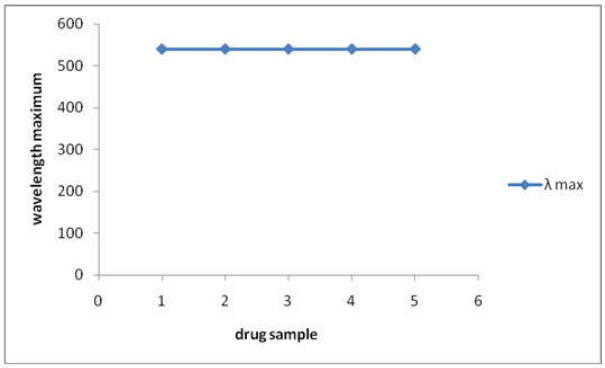

Fig. 3. Observed λ maxiumu for the drugs under study

Beers law obedience and molar absorptivity

The molar absorption coefficient, molar extinction coefficient, or molar absorptivity, denoted as ε, is a measure of absorption of light by the chemical species, at a given wavelength. It is an intrinsic property of the species and the actual absorbance, A, of a sample is dependent on the pathlength, ℓ, and the concentration, c, of the species according to Beer–Lambert law, $A = \varepsilon c \ell$. The SI units for ε are m^2/mol, but in practice, they are usually taken as M^{-1} cm^{-1} or L mol^{-1} cm^{-1}. Beer's law was found to be valid in the range 200-600µgmL^{-1} for metronidaziole, 100-300µgmL^{-1} for ornidazole, 50-300µgmL^{-1} for satranidazole, 100-600µgmL^{-1} for tinidazole and 100-500µgmL^{-1} for secinidazole. The molar absorptivity (€) for metronidazole was 72.68 cm^{-1} lit mole^{-1} ,for ornidazole was 91.14 cm^{-1} lit mole^{-1}, 3.386X10^2 cm^{-1} lit mole^{-1}, for tinidazole, 1.694X10^2 cm^{-1} lit mole^{-1}, for secinidazole and 510.2 cm^{-1} lit mole^{-1} for satranidazole. All these measurements were recorded at a wavelength maximum of 540nm. From the above data it was observed that the Beer's law obedience was found to be the least for satranidazole (Fig.4 and Fig.5).

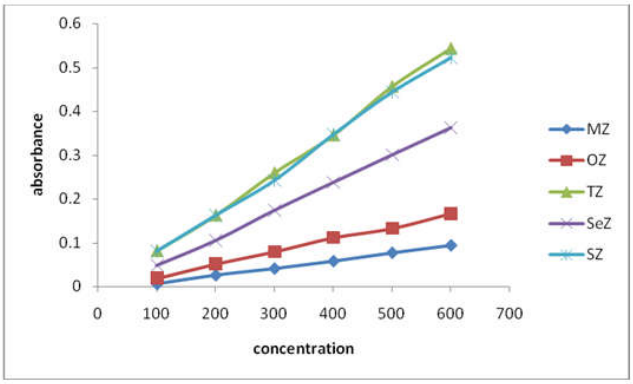

Fig. 4. Beer's law obidience plot for all the drugs under study MZ-metronidazole, OZ-ornidazole, TZ-tinidazole, SeZ-secnidazole and SZ-satranidazole

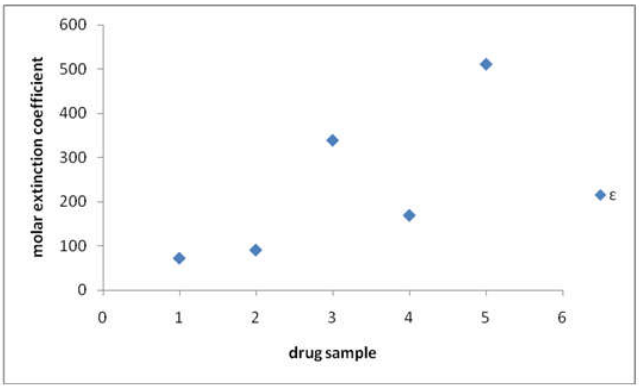

Fig. 5. Molar extinction coefficient of the drugs under study

LOD and LOQ

The lower limit of detection, or LOD (limit of detection), is the lowest quantity of a substance that can be distinguished from the absence of that substance (a *blank value*) within a stated confidence limit (generally 1%)[21-22]. LOQ is the lowest concentration at which the analyte can, not only be reliably detected, but at which some predefined goals for bias and imprecision are met. The detection limit is estimated from the mean of the blank, the standard deviation of the blank and some confidence factor. Detection limits (LOD) for metronidazole was found to be 0.01µgmL^{-1} and that for ornidazole was 0.005µgmL^{-1}. The limit of quantitation (LOQ) for metronidazole was found to be 0.04µgmL^{-1} and that for ornidazole was 0.015µgmL^{-1}. Detection limit of satranidazole was found to be 0.09 µgmL^{-1} and the limit of quantitation 0.30µgmL^{-1} .LOD for secinidazole wasfound

to be 0.02µgmL^{-1}and LOQ was 0.7µgmL^{-1}. For tinidazole the LOD was found to be 0.04µgmL^{-1} and LOQ was 0.13µgmL^{-1} (Fig.6 and Fig.7)

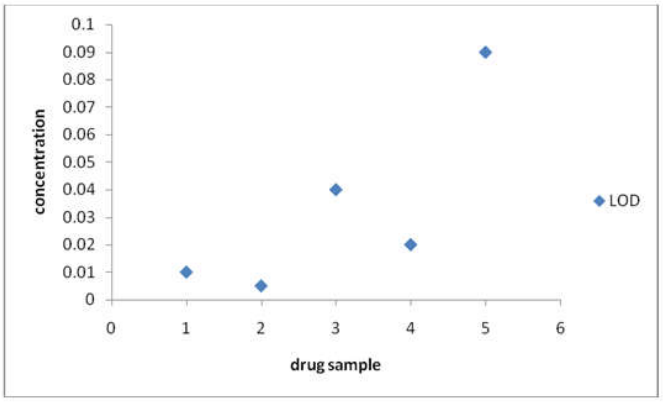

Fig. 6 . LOD (limit of detection) of the drug samples under study

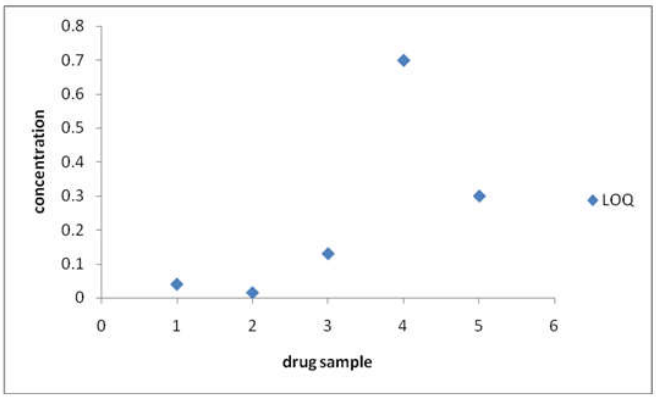

Fig. 7. LOQ (limit of quantification) of the drug samples under study

Stability

During the reaction between the above mentioned selected 5-nitroimidazole drug sample solutions and reagent solutions of 0.5% sulphanilamide and 0.3% NEDA, formation of an instantaneous stable reddish purple colored dye was observed. The stability of the resulting reddish purple coloured dye was found to be above 24 hours for all the said drugs, such as metronidazole, ornidazole, secinidazoel, tinidazole and satranidazole (Fig.8)

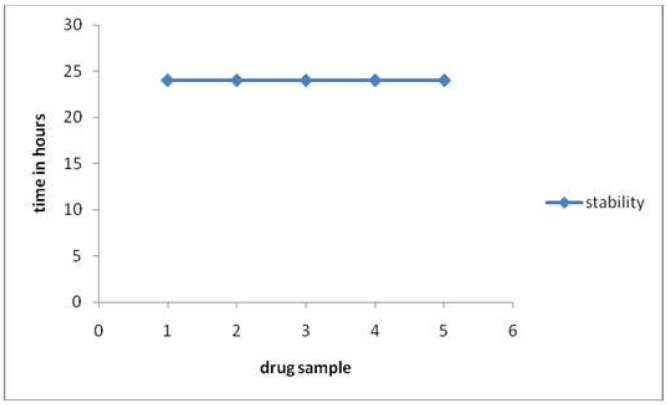

Fig. 8. Stability of the coloured product obtained by the reaction between each of the drug sample solution and the reagents specified

Correlation factor

The correlation coefficient is a measure of how well the straight line fits the analyst's data or how well a change in one variable correlates to the change in the other variable. A correlation coefficient exactly indicates the perfect linear data. The correlation factor for the drugs examined was found to be 0.9978 for metronidazole, 0.9985 for ornidazole, 0.9998 for tinidazole, 0.9990for secinidazole and 0.9994 for satranidazole (Fig.9). For each of the drug samples above, the correlation factor was found to be within the prescribed standard value.

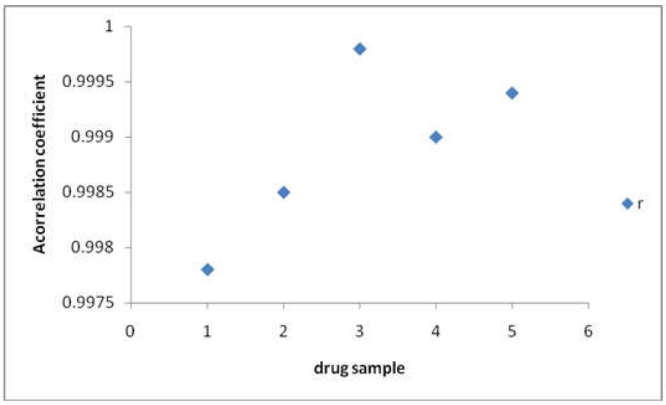

Fig. 9. Correlation coefficient of the drugs analyzed

Conclusion

A direct visible spectrophotometric method for the determinatuion of the selected 5-nitroimidazoles drugs such as metronidazole, ornidazole, secinidazoel, tinidazole and satranidazole was developed and reported. The method was found to be accurate, simple, precise with the least LOD and LOQ over all the other methods so far found in literature. It was found that all the five aforesaid drugs showed a stable, instantaneous reddish purple colored product by the reaction between the drug sample solution, 0.5% sulphanilamide and 0.3% NEDA. This direct spectrometric method developed and reported was found to be quick, accurate , precise and as such can be preferred over the earlier methods in use. The critical comparison made above confirms the accuracy, precision and superiority of the method and is an indication of identical behavior of the aforesaid drugs, in spite of the fact that their molecular weights, structural composition is different. However, the wavelength of maximum absorbance is same, indicating the probability of a common derivative product from all the above mentioned drugs.

REFERENCES

4-Nitroimidazole at Sigma-Aldrich

A.S. Amin, Anal. Lett, 30, 2503-2513 (1997).

B.A. Moussa, Int. J. Pharm. 10, 199-207 (1982).

C.S.P. Sastry, M. Aruna and A.R.M. Rao, Talanta*;*35, 23-25 (1988).

C.S.P. Sastry, M. Aruna, A.R.M. Rao and A.S.R.P. Tipirneni, Chem. Anal. (Warsaw), 36, 153-158 (1991).

D. Channe Gowda and Shankare Gowda, Ind. J. Chem. 39B, 709-711 (2000).

G .V.S.R Pavan Kumar, P Y Venkata Rao, B Krishna Kumar, V Prasanthi and B Sreerama Murty "Direct spectophotometric determination of satranidazole" Int.Jour.Pharma.Edu.Res, Vol.3, Issue.2

G.V.S.R.Pavan Kumar, T Chandra Sekhar, R G S Madhuri and B Sreeramamurty "Direct spectrophotmetric determination of tinidazole" IJABPT, Vol.2, issue 4 Oct-Dec2012.

G.V.S.R.Pavan Kumar, T Chandra Sekhar, S Satyanarayana and B Sreerama Murty "Direct spectrophotometric determination of Secnidazole" , Anal.Chem an Ind Jour, Vol.11, Issue.2 pp 56-60

Juchau, MR (1989). "Bioactivation in chemical teratogenesis". *Annu. Rev. Pharmacol. Toxicol.* 29: 165–167.doi:10.1146/ annurev.pa. 29.040189.001121.

M.L. Lopez, F.J.L. Vazquez and P.L. Lopez-de-Alba, Anal. Chim. Acta, 340, 241-244 (1997).

MacDougall, Daniel.; Crummett, Warren B.; Et Al., . (1980), "Guidelines for Data Acquisition and Data Quality Evaluation in Environmental Chemistry", *Anal. Chem.* 52: 2242–49.

Mital A (2009). "Synthetic Nitroimidazoles: Biological Activities and Mutagenicity Relationships". *Sci Pharm* 77 (3): 497–520.

N.M. Sanghavi, N.G. Joshi and D.G. Saoji, Indian J. Pharm. Sci., 41, 226-228(1979).

Nic, M.; Jirat, J.; Kosata, B., eds. (2006–). "Detection limit". *IUPAC Compendium of Chemical Terminology* .

O.S. Kamalapurkar and C. Menezes, Indian Drugs*;*22, 164 (1984).

O.S. Kamalapurkar and J.J. Chudasama, East Pharm. 26, 207-208 (1983).

P. Nagaraja, K.C. Srinivasa Murthy and H.S. Yathirajan, Talanta, 43, 1075-1080 (1996).

P. Nagaraja, K.R. Sunitha, R.A. Vasantha and H.S. Yathirajan, J. Pharm. Biomed. Anal., 28, 527-535 (2002).

R.G. Bhatkar and S.K. Chodankar, Indian J. Pharm. Sci. 42, 127-129 (1980).

T.P. Gandhi, P.R. Patel, V.C. Patel and S.K. Patel, J. Inst. Chem. 56, 127-128 (1984).

Y. Srinivasa Rao, N Suryamohana Rao, B Sreerama Murty and G.V.S.R Pavan Kumar "Direct spectrophotometric determination of metronidazole and ornidazole" Jour.Ind. Chem.Soc, Vol.89, 7, July 2012.

****