Research Article

COMPARATIVE STABILITY STUDY OF METRONIDAZOLE IN AQUEOUS AND NON AQUEOUS VEHICLE

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ABSTRACT

Metronidazole is commonly used for the treatment of *Helicobacter pylori* associated peptic ulcer. Though the Metronidazole is relatively stable with little degradation in aqueous phase but its stability is quite higher in non aqueous phase. The current article discusses about the improvement of stability of metronidazole in non aqueous vehicles which may be useful for the development of liquid formulations containing this drug. The stability study of the drug was carried out at different temperatures and relative humidity according to the ICH guidelines. It was found that the Metronidazole was about 3.7, 4.4, 4.8, 5.3 and 5.9 times more stable in 20%, 40%, 60%, 80% and 100 % v/v propylene glycol solution as compared to aqueous solution at 40^0C and 75% RH.

Keywords: metronidazole, stability, relative humidity.

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INTRODUCTION

Stability of a drug product refers to the chemical and physical integrity of the dosage unit and the ability of the drug product to maintain the concentration of its active constituents throughout the intended shelf life period. Stability testing is the main concern in the development of any formulation in pharmaceutical industries. Stability of a drug product or dosage form is one of the major problems associated with the development of liquid formulations like syrup, suspension and emulsions etc. The main objective of stability testing is to provide evidence on how the quality of drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light and to establish a re-test period for the drug substance or shelf-life for the drug product and recommended storage conditions. According to the ICH guidelines of stability testing the world is divided into four climatic zones,

I –IV, but the current stability study of Metronidazole is carried out according to the conditions of climatic zone I and II [1]. The storage conditions according to ICH guidelines are as follows:

- $25^0C \pm 2^0C$ / 60% RH ± 5% RH or $30^0C \pm 2^0C$ / 65% RH ± 5% RH for long term stability study.
- $30^0C \pm 2^0C$ / 65% RH ± 5% RH for intermediate stability study.
- $40^0C \pm 2^0C$ / 75% RH ± 5% RH for accelerated stability study.

The current article discusses about the improvement of stability of Metronidazole in non aqueous vehicles which may be useful for the development of liquid formulations containing this drug

MATERIALS AND METHODS

Materials:

Metronidazole was provided as gift sample from Lupin Laboratories, Mumbai. Propylene glycol and other chemicals were of analytical grade and were procured from CDH Laboratories, Mumbai. An UV spectrophotometer (model no. 1700) manufactured by Schimandzu, Japan was used for the analysis purpose and a Stability Chamber (Elite research, Ambala cantt.) was used for stability studies. All other facilities were provided by the institute itself

Methods:

1. Preparation of Solutions

All the solutions of Metronidazole with concentration (900 mg/100 ml) were prepared using aqueous and non aqueous vehicle. Propylene glycol used as non aqueous solvent to increases the stability of metronidazole solution [2]. Different concentrations of solvents were used for this study and the concentration of solvent varied as following types:

Sr. No.	Ingredients	Composition (% v/v)*					
		Sample 1 (S1)	Sample 2 (S2)	Sample 3 (S3)	Sample 4 (S4)	Sample 5 (S5)	Sample 6 (S6)
1.	Propylene Glycol 200	--	20	40	60	80	100
2.	Distilled Water	100	80	60	40	20	--
** All solution contains 900 mg of Metronidazole*							

Stability studies were performed according to ICH guidelines. The samples were stored in stability chamber at following conditions for a period of 12 weeks [3, 4].

$40^0C \pm 2^0C$ / 75% RH ± 5% RH and $25^0C \pm 2^0C$ / 60% RH ± 5% RH.

The samples were withdrawn every week. These samples were analyzed for drug content by UV spectrophotometer at 277 nm [5, 6]. The results thus obtained are shown as in table 1 and table 2

Table 1: Asssay of drug when stored at 40^0C with 75% RH

	Content of Drug (% Assay)												
Sample	0 Week	1 week	2 week	3 week	4 week	5 week	6 week	7 week	8 week	9 week	10 week	11 week	12 week
S1	100	77.15	79.31	76.43	71.56	63.27	51.35	43.31	34.44	29.82	22.71	17.03	13.10
S2	100	80.90	85.00	79.29	75.12	69.20	67.10	67.93	69.66	62.43	61.01	53.18	49.56
S3	100	86.89	87.08	81.79	75.75	73.10	71.19	71.96	72.43	68.13	69.08	62.91	58.36
S4	100	91.39	87.36	85.97	77.94	78.20	79.01	79.80	80.09	76.08	76.03	61.13	63.00
S5	100	94.26	87.92	89.20	79.23	83.00	89.40	86.40	85.14	80.12	78.39	69.73	70.65
S6	100	99.38	97.78	97.43	97.08	97.43	97.60	96.17	96.62	87.19	84.95	82.30	78.11
All samples stored at 40^0C with 75% RH													

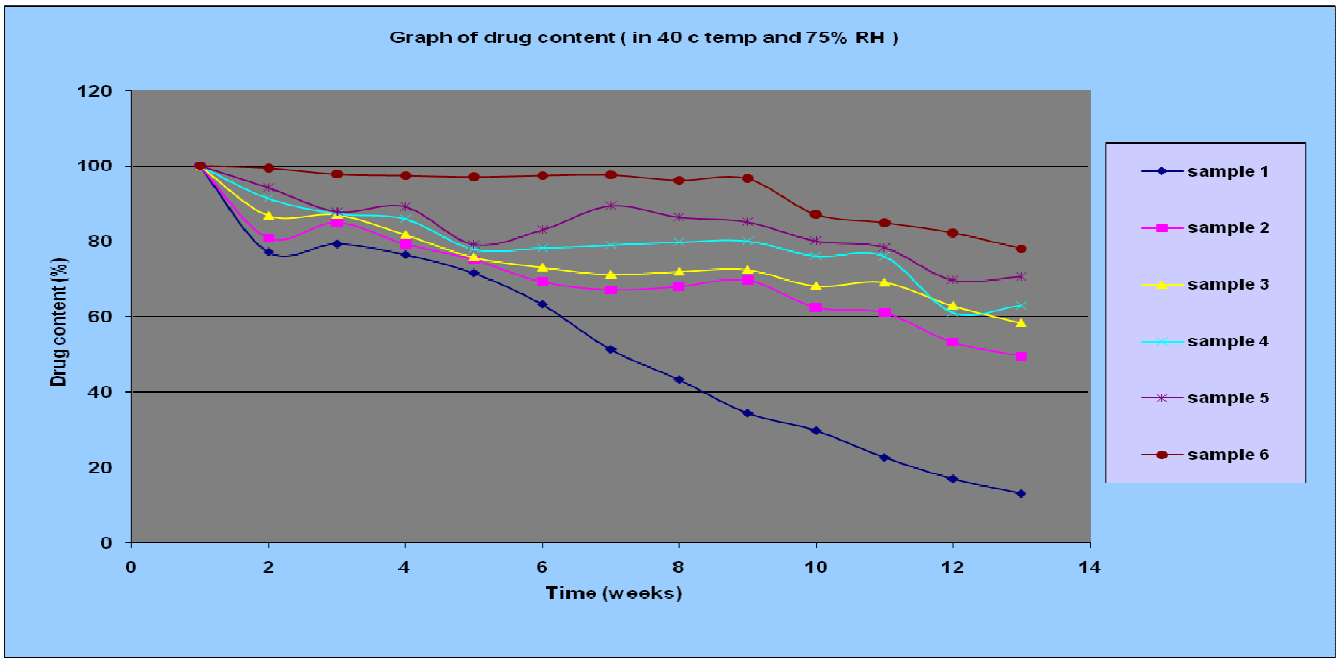
Table 2 : Assay of drug when stored at 25^0C with 60% RH

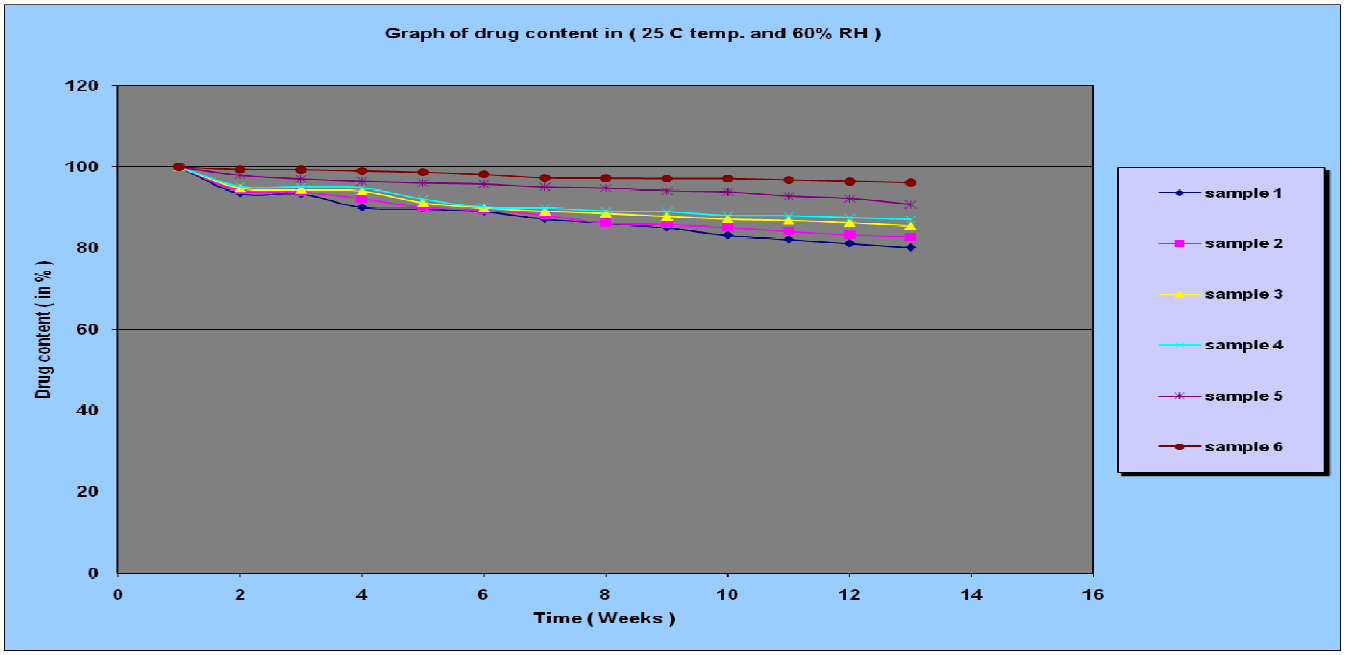
	Content of Drug (% Assay)												
Sample	0 Week	1 week	2 week	3 week	4 week	5 week	6 week	7 week	8 week	9 week	10 week	11 week	12 week
S1	100	93.43	93.33	90.01	89.66	88.97	87.19	86.21	85.01	83.17	82.09	81.12	80.12
S2	100	94.19	93.79	92.17	90.07	89.34	88.13	86.19	85.89	85.09	84.11	83.33	82.76
S3	100	94.78	94.32	93.97	91.11	89.87	89.01	88.44	87.76	87.11	86.82	86.19	85.47
S4	100	95.23	95.09	94.86	92.03	90.12	89.86	89.12	88.88	88.00	87.92	87.48	87.08
S5	100	97.92	97.01	96.41	96.01	95.78	95.03	94.78	94.10	93.79	92.78	92.19	90.79
S6	100	99.38	99.30	98.99	98.67	98.12	97.28	97.19	97.11	97.09	96.78	96.43	96.12
All samples stored at 25^0C with 60% RH													

The graphs 1 and 2 showing the content of drug decreasing with respect to time during the storage period of 12 weeks are as follows

RESULTS AND DISCUSSIONS

Stability of a drug product refers to chemical and physical integrity of the active constituents present in it. The amount of active constituents present in any formulation should not degrade until they show their therapeutic effects. To maintain these characteristics in any formulation, drug must be combined with such excipients who could maintain the integrity of the active constituents throughout its shelf life. In this current study we found that the drug Metronidazole is 3.7, 4.4, 4.8, 5.3 and 5.9 times more stable in 20%, 40%, 60%, 80% and 100 % v/v propylene glycol solution as compared to aqueous solution at 40^0C and 75% RH. From the graph 1 and 2 it is clear that the content of drug in aqueous solution is decreasing rapidly as compared with non aqueous solution using propylene glycol.





Graph 1: Assay of drug at 40^0C with 75% RH; Graph 2: Assay of drug at 25^0C with 60% RH

CONCLUSION

From the current study it is concluded that the stability of Metronidazole decreases with the aqueous vehicles and increases

with the non aqueous vehicles. Now a day the syrups solutions which are not stable in the aqueous vehicles can be prepared in non

aqueous (propylene glycol). By the use of this vehicle the stability of the solutions can be defiantly increased.

ACKNOWLEDGMENTS

The authors thanks to Head, Department of Pharmacy, Bansal College of pharmacy for providing help in carring out this work. Thanks are also due to Lupin laboratories, Mumbai for providing the active drug Metronidazole.

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