INTERNATIONAL JOURNAL OF PHARMACEUTICAL, CHEMICAL AND BIOLOGICAL SCIENCES

Available online at www.ijpcbs.com

Research Article

HYDROCHLOROTHIAZIDE: STABILITY IN BULK SOLUTION FORM

M. Ratnaparkhi* and R. Dhomse

Marathwada Mitra Mandal's College of Pharmacy, Kalewadi, Pune, Mahrashtra, India.

ABSTRACT

Present work is designed towards formulation of stable bulk solution containing thiazide diuretic like Hydrochlorothiazide. There is growing need of formulating newer and potent diuretics effectively but these drugs having some problem related to the stability in bulk form so need to solve the problem by taking batches at different temperature and check impurities at diffrent temprature (RT, 2-8^0 C, 0-5^0 C). Results shows that impurities found in bulk solution prepared at 0-5^0 C are very less as compare to bulk solution prepared at room temperature and at 2-8^0 C. Hence it is conclude that drug is unstable upon heating.

Key words: Hydrochlorothiazide; Benzothiadiazine; Degradation; Stabilty.

INTRODUCTION

Diuretics are the drug that increases the rate of urine flow, however clinically useful diuretics also increases rate of excretion of Na^+ (Natriuresis). Diuretics increase the rate of urine flow and sodium excretion and are used to adjust the volume and composition of body fluids in a variety of clinical situation, including hypertension, heart failure, nephritic syndrome and cirrhosis. Most of the diuretic agents are available as injections. The problem associated with some drug are decreased shelf life, decreased stability in solution state. Hydrochlorothiazide is stable in the solid state, undoubtadly due to its anhydrous nature. Long term storage in airtight containers has been recommended.[1] The compound in solution form undergoes hydrolytic decomposition upon standing and heating. [3] Hydrochlorothiazide undergoes hydrolysis to yield 4-amino-chloro-m-benzene disulfonamide via two series of parallel first order reaction. [1] Hydroclorothiazide is very slightly soluble in water, but readily soluble in dilute aqueous sodium hydroxide; slightly soluble in methanol and in pyridine; practically insoluble in ether, in benzene, and in chloroform.[2, 3]

EXPERIMENTAL WORK

Batch size: 100mL (each)

Common quantity added

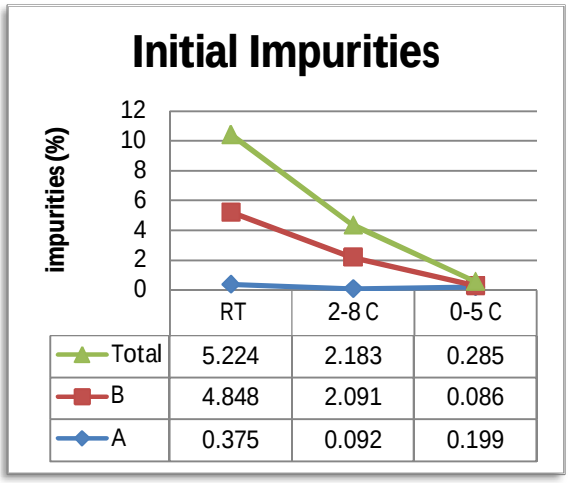
- WFI = 80mL (Initial qty)
- API = 4.206gm
- **0.5gm NaOH** used for solublization& to adjust pH (pH Limit: 9.2 to 10)
- Volume adjusted to 100mL with WFI.

Bulk solution of Hydrochlorothiazide-sodium for injection was prepared at

different temperature to check impurities and solubility of Hydrochlorothiazide. 100 mL of bulk solution prepared at RT, 2-8^{0}C and at 0-5^{0}C.Sodium hydroxide used for solublization& to adjust pH (pH Limit: 9.2 to 10) Temperature is maintained at 2-8^{0}C and at 0-5^{0}C with the help of ice bath. Care should be taken that temperature should not goes below 0^{0}C because ice crystal may be form during bulk solution preparation. Finally, bulk solution was filtered through 0.22 micron PVDF hydrophilic membrane filters. The filtered bulk solution was checked for initial analysis.

RESULT

S.No.	Experimental Trial		pH	Impurities (%)			Assay
				A	B	Total	
1	Trial at RT	Initial	9.42	0.375	4.848	5.224	97.34%
2	Trial at 2-8^0 C	Initial	9.54	0.092	2.091	2.183	98.42 %
3	Trial at 0-5^0 C	Initial	9.78	0.199	0.086	0.285	98.63%



A: Benzothiadiazine related compound,
B: Single Unknown unspecified impurity
C: Total Impurity

CONCLUSION

Description, pH, related substances and assay of sample at RT, 2-8^0 C and 0-5^0 C is observed initially. From above result and graph the Hydrochlorothiazidebulk solutionprepared at 0-5^0 C is better with impurities limitation than preparation at RT and 2-8^0 C. Impurities found at 0-5^0 are very less than impurities found at RT and 2-8^0 C. As Hydrochlorothiazide is unstable on standing or heating[1, 3]and from above table it is concluded that Hydrochlorothiazide is not stable and undergoes hydrolysis at room temperature. Hence to avoid degradation of Hydrochlorothiazide, batch should not perform at room temperature as drug is heat sensitive.

REFERENCES

1. Klaus Florey. Analytical profiles of drug substances, published by Elsevier; 18: 33-35.
2. Lawrence A. Trissel, Handbook on injectable drugs, published by American society of Health-system pharmacist, 14th edition: 359-360.

3. Marindale. The complete Drug Reference, 33rd edition, published by pharmaceutical press, 856-857, 907.
4. Krzysztof J Palucha, Lidia Tajbera, Thomas Mc Cabeb, John E O'Brienb, Owen I Corrigana and Anne Marie Healya. European Journal of Pharmaceutical Sciences.2010;41:603-611.
5. Panayotis E Macheras, Michael A. Koupparis and Sophia G Antimisiaris. Effect of temperature and fat content on the solubility of hydroHydrochlorothiazide and Hydrochlorothiazide in milk, [1]Department of Pharmacy, University of Athens, Athens 1989;10680.
6. Longer MA, Conners KA, Amidon GL and Stella VJ. Chemical Stability of Pharmaceuticals. New York: John Wiley. 1986;345-50.
7. Tucker IG, Geddes JA and Stewart PJ. Dose variations from an extemporaneously prepared Hydrochlorothiazide suspension. *Aust J Hosp Pharm*.1982;**12**:59-63
8. http://www.medscape.com