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A Review of Analytical Methods for Estimation of Amlodipin, Hydrochlorthiazide and Losartan Potassium in Pharmaceutical Formulations

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Abstract**—***Amlodipine is used in coronary artery disease, lower blood pressure, stork prevention, heart attack, kidney disease. Amlodipine belongs to a class of drug known as calcium channel blockers. Hydrochlorthiazide is a class of medication called diuretics. Losartan potassium is help protect to kidney from damages due to diabetes. It is a antagonist of angiotensin type I receptor with antihypertensive activity due to the reduced pressure effect of angiotensin II. The three drugs are used to treat high blood pressure and mainly highlight analytical study method. Techniques like UV spectrophotometry, High performance liquid chromatography, High performance thin layer chromatography, Ultra performance liquid chromatography etc. have been used for analysis Specrophotometry and High performance liquid chromatography methods have been used most widely*.

Keywords**—** *Amlodipine, Hydrochlorthiazide, Losartan potassium, UV specrophotometry, HPLC, HPTLC, and UPLC*.

I. INTRODUCTION

Amlodipine besylate (AM) is a long acting dihydropyridine calcium channel blocker effective in the treatment of angina pectoris and hypertension. Chemically it as 3-Ethyl-5-methyl(±)-2-[(2-amino ethoxy)methyl]-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5 pyrinedicarboxylate, monobenzene sulphonate. (Figure 1). Amlodipine inhibits the movement of calcium ions in to vascular smooth cells and cardiac muscle cell thereby inhibits the contraction of cardiac muscle and vascular smooth muscle cells [1].

Hydrochlorthiazide (HT) is a diuretic often used along with antihypertensive agents in the management of high blood pressure and it is also used in swelling due to fluid buildup. It is chemically 6-chloro-3,4-dihydro-2H-1,2,4-benzothiazide-7-sulfonamide 1,1-dioxide(Figure2). It reduces blood volume by acting on the kidney to reduce sodium reabsorption in the distal convoluted tubule. Additionally hydrochlorthiazide is believed to lower peripheral vascular resistance [2].

Losartan potassium (LP) is the potassium salt of losartan, a non-peptide angiotensin receptor antagonist with antihypertensive activity. Losartan, selectively and competitively binds to the angiotensin ll receptor (typeAT1) and blocks the binding of angiotensin to the receptor. It is chemically 2-butyl-4-chloro-1-[p-(0-lH-tetrarol-5-ylphenyl) benzyl] imidazol-5-methanol monopotassium salt (figure3). Losartan potassium is mainly used in the treatment of hypertension and progression of diabetic nephropathy. The chemical structure is shown in Figure 3. The above three drugs are used in combination in the treatment of high blood pressure [3].

Different methods have been reported for estimation of Amlodipine, Hydrochlorthiazide and Losartan potassium individually or in combination with other drug. In the present work, some of the recently published analytical methods for simultaneous estimation of Amlodipine, Hydrochlorthiazide and Losartan potassium are reviewed.

II. ANALYTICAL METHODS FOR ESTIMATION OF AMLODIPINE, HYDROCHLORTHIAZIDE AND LOSARTAN POTASSIUM

UV Visible Spctrophotometry

UV specrophotometric method based on simultaneous equation method and area under curve has been reported. Apart from these uv spectrophotometric by chemometric approach has also been reported. Simultaneous equation method is based upon solving simultaneous equation constructed using the absorbance measured at 3 wavelengths 236.5, 254 and 271nm, which are the absorption maxima of corresponding drugs. In the area under the curve method range of wavelength in which anyone of the drug has substantial absorption was selected. Area in this range is used for the estimation of the particular drug, accordingly 231.5-241.5nm for AML, 249-259nm for HCTZ, 266-276 nm for LOS have been chosen [4]. Specrophotometric method for simultaneous estimation of Amlodipine, Hydrochlorthaizide and Losartan potassium using chemometric tool has also been developed. Chemometric tool used was either Classical least square (CLS), Multiple linear regression (MLR), Principal component regression(PCR) or Partial test squares(PLS). Chemometric based method seem to be better analytical method for 3 drug combination with large difference in the dose and absorbtivity [5].

III. CHROMATOGRAPHIC METHODS

High Performance Liquid Chromatography

Many High performance liquid chromatography (HPLC) method were reported for the simultaneous estimation of

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Amlodipine, Hydrochlorthiazide and Losartan potassium. Mobile phase is used were the mixture of Acetonitrile in water or methanol in water, with or without buffer. The almost all the method flow rate was kept at the 1ml/min. The most of the method detector wavelength used is about 200-230nm., Which is isobestic point of Amlodipine, and Hydrochlorthiazide. In one of the methods Telmisartan is used as internal standard to increase the accuracy of the method [4]. Among the reported method lowest run time of 7.2 minute has been achieved by using mobile phase, Acetonitrile and potassium dihydrogen phosphate buffer with flow rate 1ml/min. A comparative account of the reported HPLC method is given in table 1.

TABLE 1. Comparative account of the reported HPLC method

SL. No	Drugs	Column	Mobile phase	Detector wavelength	Flow rate	Retention time	Reference
1	Amlodipine, Hydrochlorthiazide and Losartan potassium	Kromasil C8 (4.6x250mm)	Phosphate buffer:ACN (57:43 % v/v)	232nm	1.0 UP TO 6.3 MIN THEN 1.3 ml/min	AML-5.12 HCTZ-305 LOS-8.0	4
2	Amlodipne, Hydrochlorthiazide and losartan potassium	C8 column (150mmx4.6mm)	Acetonitrile and buffer (700:500 v/v)	254	1.0	AML-8.89 HCTZ-2.34 LOS-4.78	6
3	Amlodipine, Hydrochlorthiazide and Losartan potassium	Hypersil Gold Column 250x4.6 mm	Methanol: water (95:5% v/v)	230	0.8	AML-7.3 HCTZ-3.9 LOS-2085	7
4	Amlodipine, Hydrochorthiazide and Losartan potassium	C18 Column 250x4.6mm	Acetonitrile : water potassium dihydrogen phosphate buffer (60:40 % v/v)	230	1.0	AML-5.8 HCTZ-4.9 LOS-7.2	8

High Performance Thin Layer Chromatography

HPTLC is a fast separation technique and flexible and to analyze a wide variety of samples. This technique is very advantageous it is simple to handle and requires a short time to analyze. It is suitable for qualitative and quantitative analysis. Chromatographic with the advancement of the technique, high performance thin layer chromatography (HPTLC) emerged as an important instrument in technique method is summarized in Table 2.

Ultra Performance Liquid Chromatography

Ultra performance liquid chromatography (UPLC) is a new category of separation technique it is a principles of liquid chromatography. Combination of UPLC with a tandem mass spectrometer (MS/MS) appears to be a suitable approach that gives sensitivity and selectivity for the rapid determination of an analysis at low concentration in complex matrices. The technique has been applied to the method development and validation of Amlodipine, Hydrochloride and losartan potassium in bulk and in pharmaceutical dosage form. That has several advantages, including rapid analysis, a simple mobile phase, simple sample preparation and improved sensitivity and short time. The chromatographic technique method is summarized in Table 3.

TABLE 2. Chromatography methods-High performance liquid chromatography (HPTLC)

S.No	Drugs	Stationary phase	Mobile phase	Detector	Reference
1	Amlodipine, hydrochorthiazide and Losartan potasium	Silica gel plate	Chloroform:Methanol:ACN:Formic acid (7.5:1.3:0.5:0.03v/v/v/v/)	254	9

TABLE 3. Ultra performance liquid chromatography (UPLC)

S. No	Drugs	Column	Mobile phase	Flow rate	Reference
1	Amlodipine, hydrochlorothiazide and losartan potasium	C18 2.1x50mm	ACN:ammonium acetate (98:2 % v/v)	0.4 ml	10

Stability Indicating Method

Stability indicating analytical method also been reported for Amlodipine, Hydrochlorthiazide and Losartan potassium combination. The separation was achieve using C_{18} column (150mmx4.6mm), Methanol: orthophosphoric acid (65:35% v/v) as a mobile phase, flow rate (0.8ml/min) at room temperature. Stress conditions used were treating with 0.1N HCL (Acid stress), 0.1N NaOH (Alkaline stress), 5%v/v hydrogen peroxide (oxidative stress) for 24 hrs. Samples for photolytic stress are placed in a transparent glass vial and placed in a UV chamber for 24 hrs. In developed analytical method the degradation product did not interfere with analytic signals. Stress studies indicated that hydrochlorthiazide is not susceptible to degradation under acid, oxidative stress, light (UV) stress conditions. However, in alkaline conditions (0.1N NaOH), the drug was unstable and the degradation peak eluted later accompanied with a drastic peak distortion and increased tailing. Except for alkaline conditions, drug content was within the range 98.04-98.84% for all stress conditions which indicate its stability also the analytical method is specific to differentiate the degradation peaks. Stress studies on amlodipine besylate indicated that it was stable under acidic, oxidative stress and light (UV) conditions. However, in alkaline conditions (0.1N NaOH), the drug was unstable. It was seen that degradation peak eluted later and accompanied with a peak distortion, increased tailing. In all the stress conditions, the drug content of amlodipine besylate was within 95.19-99.11% which indicating the stability and also the analytical method is specific and differentiate the degradation

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peaks. In case of stress studies Losartan potassium indicated that it was stable under acidic, oxidative stress and light (UV). In alkaline conditions (0.1N NaOH), the drug was unstable and the degradation peak eluted later. In all stress conditions, the drug content of Losartan potassium was within 96.96-98.23% indicating the stability and also the analytical method is to specific and differentiate the degradation peaks [11].

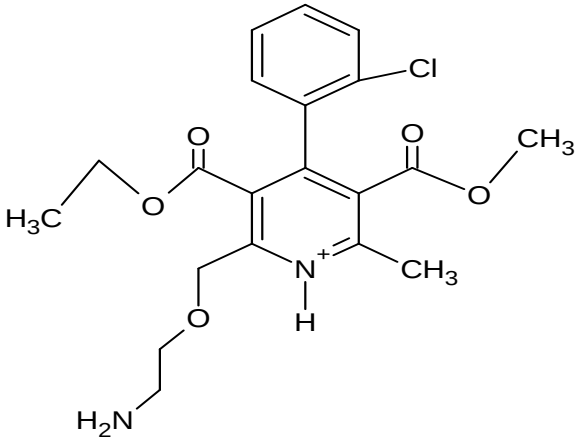

Fig. 1. Chemical structure of Amlodipine

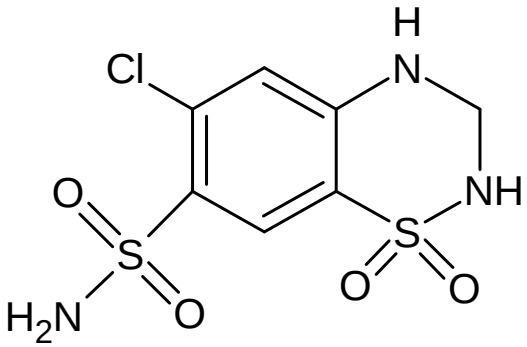

Fig. 2. Chemical structure of Hydrochlorthiazide

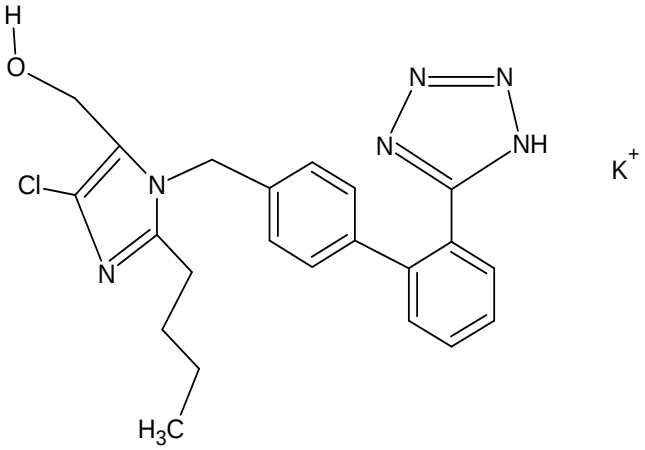

Fig. 3. Chemical structure of Losartan potassium

IV. CONCLUSION

The review of literature survey reveal that various analytical methods available for estimation of Amlodipine, Hydrochlorthiazide and Losartan potassium. Whether reported by one of the methods Telmisartan is used as internal standard to increase the accuracy of the method. Among the reported method lowest run time of 7.2 minute has been achieved by using mobile phase, Acetonitrile and potassium dihydrogen phosphate buffer with flow rate 1ml/min. HPLC method is frequently used because of high sensitivity , specificity, and better separation efficiency. However there is no report based on scientific approach using Design of Experiment. Which may give better experimental parameters. These chromatographic methods are rapid and far more economical. The presented information is useful for the researchers.

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