Literature review on method development for drug combinations specifically selected for present work:

1) Literature Review for the combination of Losartan potassium and Enalapril maleate:

There are only three methods reported so far, for estimating Losartan potassium and Enalapril maleate in their combination formulations. The reported methods are two High performance LC methods and only one UV spectrophotometric method i.e. technique of simultaneous equation. Therefor; intention of the current research was the development of some accurate, simplest and economically feasible first-order derivatization spectrometric techniques for the rapid investigation of Losartan potassium and Enalapril maleate in bulk drugs and combination tablets formulations.

- Thomas, Chaudhary, Nanda and Chavan (2009) developed two simultaneously quantitation methods for Losartan potassium and Enalapril maleate in medicinal formulation products by UV-spectrophotometric methods and Liquid Chromatography. The foremost technique includes spectrometric analysis using the simultaneous formula set of equations processing at 222nm and 250nm for Enalapril and Losartan. In the next method RPLC column with mobile-phase composed of methanol, water, Acetonitrile in the ratio of 45:35:20 was used for the determination.

This first method reported by these authors employs solving of simultaneous equations at the employed wavelengths for the investigation of Losartan and Enalapril. The method is simple, but the rapidity and accuracy are not reliable. Simultaneous equation methods yield accurate results only if the zero order spectrums of all the drugs under investigation show clearly separated absorption maxima i.e. the absorption spectrum of all drugs under evaluation should not be overlapping. The authors do not provide any evidence relating absorption spectrum and details about overlain spectrum. Another factor of inconvenience is the range of simultaneous equations, i.e. the solving of simultaneous equations holds well within a given range for the particular drug combination selected.
The method is based on lengthy calculations and the method demands the use of absorptivities along with absorbances. This makes the method to lag behind when rapidity is the major criteria. The method employs methanol as the only solvent and no other reagent is required. The method utilizes very limited number of apparatus, i.e. routine laboratory glasswares used for dilutions purposes whereas the chromatographic techniques demand costly reagents, solvents and chemicals.

The second reported method is a High performance LC method for the investigation of Losartan and Enalapril, and always the method of choice when accuracy is the primary factor. The method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.

High performance LC and Ultra Violet techniques of analysis are the favorite methods of a hundreds of authors and their co-workers because of their accuracy, rapidness and applicability for the regular investigation of various drugs in their combined dosage forms. Literature for the present study is given in brief as under. In most of the cases, High performance LC is the method of choice wherever the highest accuracy is preferred although it is an expensive technique, but it has the advantage of separation of the components also; it is the needed criteria where isolation and characterization is critical and Ultra Violet spectrophotometric techniques fall apart therein. When cost effectiveness is the preferred criteria over highest accuracy, then ultra violet spectrophotometric techniques have an important role to play, and occupy the second spot after High performance LC techniques, when isolation and characterization of the products is not necessarily the requirement of the analysis.

- Patel (2013) reported a validated method for the quantitation of Enalapril maleate and Losartan potassium simultaneously drugs in bulk and medicinal formulations. The reported method was a High performance LC method with good accuracy and precision.
The reported method is a High performance LC method for the investigation of Losartan and Enalapril, and always the method of choice when accuracy is the primary factor. The method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.

2) Literature Review for the combination of Olmesartan medoxomil and Ramipril:

Only four methods are reported so far including two liquid chromatographic methods and one absorption factor correction method for the simultaneous investigation of Olmesartan medoxomil and Ramipril in their combination formulations and one first-order derivative spectrophotometric technique. Aim was the present attempt was the investigation of an easy, economically less expensive and rapid First derivatization technique for the quantitization of these drugs in combination using other instrument alternative to the instrument used in the reported method.

- Patel, Khandhar, Captain and Patel (2007) reported two analytical processes for the quantitative investigation of Ramipril and Olmesartan in multicomponent dosage forms. The first method involves the determination of these drugs by Absorption factor spectrophotometric method where Ramipril was measured at 210nm and Olmesartan at 256nm in the Beer’s-limits of 2-6µg per ml and 8-24µg per ml respectively. In the second method H.P.L.C. technique was followed for the quantitization of these drugs in medicinal preparations using mobile-phase consisting sodium per chlorate and Acetonitrile in the ratio 60:40 with UV-visualization at 210nm. Phenomenex C8 was used as stationary phase. Beers range was 1-6 and 4-24µg/ml for Ramipril and Olmesartan respectively.

The first method involves the use of absorption factor correction method for the quantitization of the drug combination of Olmesartan and Ramipril. As discussed in the early sections, the method requires lengthy calculations and calculation of absorptivities
along with measurement of absorbances of each component. This method is also not a very accurate method because the calculations provide fractions rather than concentration. Otherwise, the method is simple, convenient and be used when routine methods demand its application. The method employs methanol as the only solvent and no other reagent is required. The method utilizes very limited number of apparatus, i.e. routine laboratory glasswares used for dilutions purposes whereas the chromatographic techniques demand costly reagents, solvents and chemicals.

The second method is a High performance LC method for the investigation of Ramipril and Olmesartan, and always the method of choice when accuracy is the primary factor. The method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.

High performance LC and Ultra Violet techniques of analysis are the favorite methods of a hundreds of authors and their co-workers because of their accuracy, rapidness and applicability for the regular investigation of various drugs in their combined dosage forms. Literature for the present study is given in brief as under. In most of the cases, High performance LC is the method of choice wherever the highest accuracy is preferred although it is an expensive technique, but it has the advantage of separation of the components also; it is the needed criteria where isolation and characterization is critical and Ultra Violet spectrophotometric techniques fall apart therein. When cost effectiveness is the preferred criteria over highest accuracy, then ultra violet spectrophotometric techniques have an important role to play, and occupy the second spot after High performance LC techniques, when isolation and characterization of the products is not necessarily the requirement of the analysis.

- Karajgi, Simpi and Kalyane (2012) developed a simultaneous UV estimation method for Ramipril and Olmesartan. Ramipril was determined at 240nm and Olmesartan was
determined at 246nm. The method was validated and linearity was determined by the method of least squares (Jeffery et al., 1994b).

The reported method is an ideal method for the routine investigation of the stated combination of drugs. It offers accuracy, precision, sensitivity, selectivity, applicability for routine purposes and has many advantages over zero order spectrophotometric methods. The reported method is simple and rapid method with the conversion of zero order absorption spectrum to first order derivative spectrum automatically with the help of instrumental processing of spectrum.

The drugs were subjected to analysis after getting appropriate dilutions of standard solutions, applied on both bulk drugs and formulations availed from market. The authors claim that the method shows linearity in the employed range with satisfactory accuracy and precision.

The advantage chief of the above work is its simplicity, because the instrument described is easy to handle. The other advantage is its applicability for the routine analysis for various routine investigations like dissolutions studies, rate determinations studies, release studies, Pharmaco-kinetic studies, bioavailability studies and other common day to day evaluations. Another application of this technique is its cost-effectiveness and it is the primary advantage over high performance liquid chromatographic methods of analytical investigation. The method employs methanol as the only solvent and no other reagent is required. The method utilizes very limited number of apparatus, i.e. routine laboratory glasswares used for dilutions purposes whereas the chromatographic techniques demand costly reagents, solvents and chemicals.

- Patil and Shinde (2011) developed a Liquid Chromatographic stability indicative scheme for the analysis of Olmesartan and Ramipril simultaneously in pharmaceutical formulations. In this method, a chromatographic separation was achieved with YMC pack O.D.S. analytical column as stationary phase and buffers, Acetonitrile and methanol in the ratio of 50:40:10 as the mobile-phase adjusted up to pH 3.0 using trifluoro acetic
acids. 0.1M sodium per chlorate monohydrate was used as buffer. Detection wavelength was 210nm.

The method reported by these authors for the regular determination of Olmesartan and Ramipril is an excellent method for the specific and selective determination of the drug combination of Olmesartan and Ramipril in presence of impurities associated with their synthetic pathways and in presence of even their degradation products. The method is a stability indicating method. The active ingredients were subjected to degradation procedures like oxidation, hydrolysis, photolysis and heat as the stress conditions to prove the linearity of the method.

The method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.

- Rao, Velrajan and Sekhar (2013) developed a R.P.-H.P.L.C. method for the quantitization of Ramipril and Olmesartan simultaneously in tablets formulations using an inert sil C8 column as stationary phase with a mobile-phase mixture of mixed phosphate buffer of pH-6.8 with Acetonitrile in the proportion of 65:35. The drugs were detected at 219nm and the retention time were 2.28 minutes for Ramipril and 3.76 minutes for Olmesartan.

The second method is a High performance LC method for the investigation of Ramipril and Olmesartan, and always the method of choice when accuracy is the primary factor. The method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.
3) Literature Review for the combination of Ramipril and Amlodipine besylate:

Literature review reveals that there are only few methods reported for the simultaneously quantitation in the combined multicomponent formulations of Ramipril and Amlodipine. The reported methods include four High performance LC methods, two TLC methods and one UV spectrophotometric absorbance ratio method and no First derivatization spectrophotometric method is still described for the simultaneously quantitation of the presently selected drugs in their combined pharmaceutical formulations. Therefore, the purpose of the present investigation was to find a simultaneously quantitation technique for the analysis of Ramipril and Amlodipine in dosage products and bulk synthetic mixtures.

- Bhushan, Gupta and Singh (2005) reported LC based separation and UV-spectrophotometric investigation of some selected anti-hypertensive agents. Active ingredients were separated from binary formulations by RP-High performance LC method using methanol-water (50:50v/v) and by TLC using Chloroform-methanol (6:1) as mobile phase. UV detection was at 210nm by High performance LC and Iodine vapors in TLC.

The first method is a High performance LC method for the investigation of Ramipril and Amlodipine, and always the method of choice when accuracy is the primary factor. The method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.

The second method is a conventional thin layer chromatography method, which is too traditional and fundamental technique which is basically is a preparatory technique and not a method suitable for direct quantitization of pharmaceuticals. It is an outdated technique useless for simultaneously quantitization for routine purpose and a better technique for isolation, separation and characterization rather than estimation of these drugs in medicinal dose forms.
Patil, Rakesh, Dhabale and Burade (2009) reported simultaneous quantitation of Ramipril and Amlodipine by Ultra-Violet spectrophotometry technique. The method was based on absorbance-ratio analytical process which involves the measurement of absorbance at separate wavelengths at 210nm and 238nm for Ramipril and Amlodipine correspondingly. Method linearity was observed in the quantification range of 5-35µg per ml for Ramipril and 5-25µg per ml for Amlodipine.

The method involves the use of absorption factor correction method for the investigation of Ramipril and Amlodipine. As discussed in the early sections, the method requires lengthy calculations and calculation of absorptivities along with measurement of absorbances of each component. This method is also not a very accurate method because the calculations provide fractions rather than concentration. Otherwise, the method is simple, convenient and be used when routine methods demand its application. The method employs methanol as the only solvent and no other reagent is required. The method utilizes very limited number of apparatus, i.e. routine laboratory glasswares used for dilutions purposes whereas the chromatographic techniques demand costly reagents, solvents and chemicals.

Shah, Jaydeep, Kashyap, Sunil and Us mangani (2012) developed a High performance thin layer chromatographic (HPTLC) estimation scheme for the simultaneous quantitization of Amlodipine besylate and Ramipril in medicinal formulations. Thin Layer Chromatographic plates pre-coated with Silica-gel G60 F254 used as stationary phase and methanol: ethyl acetate: toluene: ammonia (2.5:3.5:4:0.2 v/v) as mobile-phase. Densitometric identification was followed at 210nm. The retention factors determined for Amlodipine and Ramipril were correspondingly 0.43 and 0.63 in that order. The method showed linearity in the quantification series of 500-3000ng per spot for Amlodipine besylate and 250-1500 per spot for Ramipril.

The method is a HPTLC method for the separative estimation of Ramipril and Amlodipine, a technique of similar accuracy as of spectrophotometric techniques. The
advantage of the technique is that the process is rapid i.e. fast method which is less time consuming. The method shows good accuracy, precision, above all sensitive than thin layer chromatography. The disadvantage of the method is requirement of skills, costly reagents. The drawback of the method is its lack of application for routine methods of investigation.

- Rajput, Kaur, Gill, Mittal and Sarma (2012) established a method for the simultaneous analysis of Ramipril and Amlodipine drugs in bulk and in tablets preparations by Reverse Phase-High performance LC technique. C18 column was used as stationary phase and 50:20:25 v/v/v ratio of Acetonitrile, Sodium phosphate buffer and Methanol mobile phase. The retention periods were 2.64 minutes for Ramipril and 7.45 minutes for Amlodipine. The linearity of calibration plots was found to be in the determinable concentrations of 1-16µg per ml and 0.2-3.2µg per ml for Ramipril and Amlodipine respectively.

The first method is a High performance LC method for the investigation of Ramipril and Amlodipine, and always the method of choice when accuracy is the primary factor. The method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.

- Kumar, Vijay, Nasare, Rao, Prasad and Diwan (2012) carried out the estimation of Ramipril and Amlodipine in pharmaceutical product formulations by Isocratic R. P.-High Performance Liquid Chromatographic method. The separation was successful using a Phenomenex C18 column as stationary phase and buffer of mixed phosphate: Acetonitrile (60:40 v/v) mobile phase, with Ultra-Violet visualization at 237nm. The retention times of Ramipril and Amlodipine were 2.13 minutes and 5.18 minutes correspondingly. The method is a High performance LC method for the investigation of Ramipril and Amlodipine, and always the method of choice when accuracy is the primary factor. The
method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.

- **Dai, Qiu, Wu and Fu (2013)** developed a validated Reverse Phase-High performance LC scheme for simultaneous analysis of Ramipril and Amlodipine in tablet products. The assay was stability indicating and validated as per Chinese Pharmacopoeia. The method was linear in the analytical range of 0.01µg per ml to 0.25 µg per ml for Ramipril and 0.014 µg per ml to 0.36µg per ml for Amlodipine. Triethanolamine-acetonitrile with Sodium per chlorate buffer (60:40) was used as mobile phase (A) and Triethanolamine-acetonitrile with Sodium per chlorate buffer (20:80) as mobile phase (B) for gradient elution. Inertsil ODS-3 column as stationary phase.

The method is a High performance LC method for the investigation of Ramipril and Amlodipine, and always the method of choice when accuracy is the primary factor. The method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.

- **Venkatesh, Chowdary, Harita, Anuroop and Reddy (2013)** reported a reverse phase LC estimation technique for the simultaneous evaluation of Ramipril and Amlodipine in formulations. The separation attained with mixed phosphate buffer and Acetonitrile (40:60) mobile phase and C18 column as stationary phase. Detection wavelength was 230nm with retention time of Ramipril and Amlodipine 3.43 and 3.99minutes.

The method is a High performance LC method for the investigation of Ramipril and Amlodipine, and always the method of choice when accuracy is the primary factor. The
method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.

4) Literature Review for the combination of Olmesartan medoxomil and Amlodipine besylate:

Study of literature show that a number of schemes are reported for the analysis of Olmesartan medoxomil and Amlodipine besylate for simultaneously quantitizations. Six High performance LC methods, one HPTLC method, six UV spectrophotometric methods including multivariate spectrophotometric, technique of area under curve, technique of simultaneous equation and two First derivatization spectrophotometric methods were reported for the investigation of Olmesartan medoxomil and Amlodipine besylate simultaneously in the combination multicomponent formulations.

- Mehulkumar, Ramesh, Kumar, Vinay, Srinivas and Diwan (2009) reported simultaneous spectrophotometric method for the analysis of Amlodipine besylate and Olmesartan medoxomil in tablets preparations. The technique employed for the investigation was first order zero crossing method using Acetonitrile as the solvent where Olmesartan shows zero crossing at 259nm and Amlodipine shows zero crossing at 237nm. Linear concentration range was 5-30µg per ml each for Amlodipine and Olmesartan.

The reported method is an ideal method for the routine investigation of the stated combination of drugs for the quantitative evaluation of Olmesartan medoxomil and Amlodipine besylate. It offers accuracy, precision, sensitivity, selectivity, applicability for routine purposes and has many advantages over zero order spectrophotometric methods. The reported method is simple and rapid method with the conversion of zero
order absorption spectrum to first order derivative spectrum automatically with the help of instrumental processing of spectrum.

The drugs were subjected to analysis after getting appropriate dilutions of standard solutions, applied on both bulk drugs and formulations availed from market. The authors claim that the method shows linearity in the employed range with satisfactory accuracy and precision.

The advantage chief of the above work is its simplicity, because the instrument described is easy to handle. The other advantage is its applicability for the routine analysis for various routine investigations like dissolutions studies, rate determinations studies, release studies, Pharmaco-kinetic studies, bioavailability studies and other common day to day evaluations. Another application of this technique is its cost-effectiveness and it is the primary advantage over high performance liquid chromatographic methods of analytical investigation. The method employs methanol as the only solvent and no other reagent is required. The method utilizes very limited number of apparatus, i.e. routine laboratory glasswares used for dilutions purposes whereas the chromatographic techniques demand costly reagents, solvents and chemicals.

The only and major disadvantage of this method is the corrosive, toxic and harmful hazardous nature of Acetonitrile and of course, it is a costlier affair to use for routine purpose. Except this disadvantage, the method is better relevant for the routine applications.

- Wankhede, Wadkar, Raka and Chitlange (2009) reported two spectrophotometric methods and one High performance LC method for the quantitation of Amlodipine besylate and Olmesartan medoxomil simultaneously in medicinal formulations. Initial spectrophotometric technique was carried out by employing simultaneous- formula at 237.5nm and 255.5nm in the analytical range 10-50µg per ml for both drugs. For the second method, technique of area under curve was applied at the wavelengths of 242nm-232.2nm and 260.5nm-250.5nm for Amlodipine and Olmesartan in the quantitative range
of 10-50µg per ml for both drugs. Third process was a High performance LC technique employing Kromasil RP C18 column and mobile-phase composed of 0.05M mono-potassium dihydrogen phosphate and Acetonitrile (50:50) with detection wavelength of 238nm.

This first method reported by these authors employs solving of simultaneous equations at the employed wavelengths intended for the analytical quantitization of Olmesartan medoxomil and Amlodipine besylate. The method is simple, but the rapidity and accuracy are not reliable. Simultaneous equation methods yield accurate results only if the zero order spectrums of all the drugs under investigation show clearly separated absorption maxima i.e. the absorption spectrum of all drugs under evaluation should not be overlapping. The authors do not provide any evidence relating absorption spectrum and details about overlain spectrum. Another factor of inconvenience is the range of simultaneous equations, i.e. the solving of simultaneous equations holds well within a given range for the particular drug combination selected. The method is based on lengthy calculations and the method demands the use of absorptivities along with absorbances. This makes the method to lag behind when rapidity is the major criteria. The method employs methanol as the only solvent and no other reagent is required. The method utilizes very limited number of apparatus, i.e. routine laboratory glasswares used for dilutions purposes whereas the chromatographic techniques demand costly reagents, solvents and chemicals.

The second method reported by these authors is a technique of area under curve intended for the analytical quantitization of Olmesartan medoxomil and Amlodipine besylate. This method like absorption factor correction method yields fractions rather than concentrations, which makes the method less accurate compared to the other types of ultraviolet spectrophotometric methods. This method is also not a very accurate method because the calculations provide fractions rather than concentration. Otherwise, the method is simple, convenient and be used when routine methods demand its application. The method employs methanol as the only solvent and no other reagent is required. The method utilizes very limited number of apparatus, i.e. routine laboratory glasswares used
for dilutions purposes whereas the chromatographic techniques demand costly reagents, solvents and chemicals.

The third reported method is a High performance LC method intended for the analytical quantitization of Olmesartan medoxomil and Amlodipine besylate, and always the method of choice when accuracy is the primary factor. The method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.

High performance LC and Ultra Violet techniques of analysis are the favorite methods of a hundreds of authors and their co-workers because of their accuracy, rapidness and applicability for the regular investigation of various drugs in their combined dosage forms. Literature for the present study is given in brief as under. In most of the cases, High performance LC is the method of choice wherever the highest accuracy is preferred although it is an expensive technique, but it has the advantage of separation of the components also; it is the needed criteria where isolation and characterization is critical and Ultra Violet spectrophotometric techniques fall apart therein. When cost effectiveness is the preferred criteria over highest accuracy, then ultra violet spectrophotometric techniques have an important role to play, and occupy the second spot after High performance LC techniques, when isolation and characterization of the products is not necessarily the requirement of the analysis.

- Sharma T, Mishra, Sudam and Shankar (2010) reported two methods for the simultaneous assay of Olmesartan medoxomil and Amlodipine besylate in medicinal dosage forms by Ultra-Violet spectrophotometric processing. Initial technique was carried out by the use of simultaneous-formula and second method was processed by Q-value procedure. The methods involved the solving of simultaneous equation and absorptivity values at 256.8nm, 239nm and 235.6nm. The methods showed linearity between the quantitization limits of 5-30µg/ml for each drugs.
This first method reported by these authors employs solving of simultaneous equations at the employed wavelengths for the investigation of Amlodipine and Olmesartan. The method is simple, but the rapidity and accuracy are not reliable. Simultaneous equation methods yield accurate results only if the zero order spectrums of all the drugs under investigation show clearly separated absorption maxima i.e. the absorption spectrum of all drugs under evaluation should not be overlapping. The authors do not provide any evidence relating absorption spectrum and details about overlain spectrum. Another factor of inconvenience is the range of simultaneous equations, i.e. the solving of simultaneous equations holds well within a given range for the particular drug combination selected. The method is based on lengthy calculations and the method demands the use of absorptivities along with absorbances. This makes the method to lag behind when rapidity is the major criteria. The method employs methanol as the only solvent and no other reagent is required. The method utilizes very limited number of apparatus, i.e. routine laboratory glasswares used for dilutions purposes whereas the chromatographic techniques demand costly reagents, solvents and chemicals.

The second method involves the use of absorption factor correction method for the investigation of Amlodipine and Olmesartan. As discussed in the early sections, the method requires lengthy calculations and calculation of absorptivities along with measurement of absorbances of each component. This method is also not a very accurate method because the calculations provide fractions rather than concentration. Otherwise, the method is simple, convenient and be used when routine methods demand its application. The method employs methanol as the only solvent and no other reagent is required. The method utilizes very limited number of apparatus, i.e. routine laboratory glasswares used for dilutions purposes whereas the chromatographic techniques demand costly reagents, solvents and chemicals.

- Kamble, Mahadeo, Khatal and Dhaneshwar (2010) developed a validated H.P.L.C. and H.P.-T.L.C. methods for the quantitization of Amlodipine besylate and Olmesartan medoxomil simultaneously in drugs in bulk and medicinal dosage forms. The primary
scheme was processed on the H.P.-T.L.C. partition of Amlodipine besylate and Olmesartan medoxomil using Merck Aluminium HPTLC papers of silica gel 60 F 254 stationary phase and n-butanol:acetic acid:water in the ratio of 5:1:0.1 v/v/v as mobile phase. The second technique was based on H.P.L.C. division of these components on the RP-perfectsil 100 ODS 3-C18 column as stationary phase and Acetonitrile/0.03M ammonium acetate buffer adjusted with pH3 in a share of 55:45 as the mobile phase.

The first reported method is a High performance LC method for the simultaneous quantitization of Olmesartan and Amlodipine, and always the method of choice when accuracy is the primary factor. The method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.

The second method is a HPTLC method for the separative estimation of Amlodipine and Olmesartan, a technique of similar accuracy as of spectrophotometric techniques. The advantage of the technique is that the process is rapid i.e. fast method which is less time consuming. The method shows good accuracy, precision, above all sensitive than thin layer chromatography. The disadvantage of the method is requirement of skills, costly reagents. The drawback of the method is its lack of application for routine methods of investigation.

- Patil, Rane, Sangshetti, Yeole and Shinde (2010) developed a stability indicating LC method for the quantitization of Amlodipine and Olmesartan simultaneously in pharmaceutical products. A chromatographical separating of these components was attained with an ACE 5 C18 Column stationary phase and buffer: Acetonitrile 60:40 v/v mobile phase. The method exhibited linear results in the series of 20-400μg per ml for Olmesartan and 5-100μg per ml for Amlodipine.
The method reported by these authors is an excellent method for the specific and selective determination of the antihypertensive drugs Amlodipine and Olmesartan in presence of impurities associated with their synthetic pathways and in presence of even their degradation products. The method is a stability indicating method. The active ingredients were subjected to degradation procedures like oxidation, hydrolysis, photolysis and heat as the stress conditions to prove the linearity of the method.

The method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.

- Kardile, Patel and Patel (2011) reported two methods for the quantization of Amlodipine besylate and Olmesartan medoxomil in their combined preparations simultaneously by H.P.L.C. and Ultra-Violet spectrophotometric techniques. The first scheme was a UV processing scheme using simultaneous formula processing at 239nm and 256nm in a determination range of 15µg/ml for both drugs. The second scheme was carried out on the basis R.P.-H.P. Liquid chromatographic analysis using 0.05M potassium dihydrogen phosphate: Acetonitrile 50:50 v/v mobile phase and C18 bonded stationary phase. The UV detection was achieved from 230nm-260nm. The method was linear at 5-20µg/ml for both drugs. Retention period of Olmesartan medoxomil was observed as 5.36 minutes and for Amlodipine besylate 3.69 minutes.

The first reported method is a High performance LC method for the simultaneous quantitization of Olmesartan and Amlodipine, and always the method of choice when accuracy is the primary factor. The method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.
The second reported method is an ideal method for the routine investigation of the stated combination of drugs for the quantitative evaluation of Olmesartan medoxomil and Amlodipine besylate. It offers accuracy, precision, sensitivity, selectivity, applicability for routine purposes and has many advantages over zero order spectrophotometric methods. The reported method is simple and rapid method with the conversion of zero order absorption spectrum to first order derivative spectrum automatically with the help of instrumental processing of spectrum.

The drugs were subjected to analysis after getting appropriate dilutions of standard solutions, applied on both bulk drugs and formulations availed from market. The authors claim that the method shows linearity in the employed range with satisfactory accuracy and precision.

The advantage chief of the above work is its simplicity, because the instrument described is easy to handle. The other advantage is its applicability for the routine analysis for various routine investigations like dissolutions studies, rate determinations studies, release studies, Pharmaco-kinetic studies, bioavailability studies and other common day to day evaluations. Another application of this technique is its cost-effectiveness and it is the primary advantage over high performance liquid chromatographic methods of analytical investigation. The method employs methanol as the only solvent and no other reagent is required. The method utilizes very limited number of apparatus, i.e. routine laboratory glasswares used for dilutions purposes whereas the chromatographic techniques demand costly reagents, solvents and chemicals.

However, after going through the publication, some contrast statements were confusing and obviously, the faithfulness of authors may be suspected and the method seems to be a non genuine and original work. Therefore, there is a need of verification of the reported work.

- Patil, Chivate, Shinde, More and Pishwikar (2011) reported a simultaneous method for the analysis of Olmesartan medoxomil and Amlodipine besylate from tablets products by
multi wavelength process. The solutions of these drugs were scanned between 265, 324 and 360nm as wavelengths. For Olmesartan medoxomil, the interfering because of Amlodipine besylate was reduced by absorbance difference at 265 and 324nm where as quantification of Amlodipine besylate at 360nm. The method obeys Beer-Lambert’s law of linearity over the determination range of 2-32µg per ml for Olmesartan medoxomil and 2-20µg per ml for Amlodipine besylate.

The method involves the use of absorption factor correction method for the investigation of Amlodipine and Olmesartan. As discussed in the early sections, the method requires lengthy calculations and calculation of absorptivities along with measurement of absorbances of each component. This method is also not a very accurate method because the calculations provide fractions rather than concentration. Otherwise, the method is simple, convenient and be used when routine methods demand its application. The method employs methanol as the only solvent and no other reagent is required. The method utilizes very limited number of apparatus, i.e. routine laboratory glasswares used for dilutions purposes whereas the chromatographic techniques demand costly reagents, solvents and chemicals. Another absorption ratio method is already has been reported for the same combination of drugs.

- Patil, More and Pishawikar (2011) developed Reverse-Phase H.P.L.C. technique for the quantitization of Amlodipine besylate and Olmesartan medoxomil simultaneous in tablets preparations. The separation of components was resolved using Acetonitrile-water (60:40 v/v) mobile-phase. The linearity graph obtained in the quantitation range of 5-35µg per ml for both drugs.

The reported method is a High performance LC method for the simultaneous quantitization of Olmesartan and Amlodipine, and always the method of choice when accuracy is the primary factor. The method is comparatively better than ultraviolet spectrophotometry, but major disadvantage is its non economical effect, when routine determinations are the processes of investigation. The method shows good linearity as
the authors claim. There are many other High performance LC methods are reported by different authors for the same combination of drugs.

- Kawade, Shah and Asnani (2012) reported multicomponent type analytical method for Olmesartan medoxomil and Amlodipine besylate in combined tablets formulations by Ultra-Violet spectrophotometry. The method was developed using multicomponent mode on Shimadzu 1601 model spectrophotometer. The drugs were determined at 256nm for Olmesartan and 364nm for Amlodipine. The linearity for both drugs was found to be 2-20µg/ml.

The reported method is an outdated conventional and very traditional method for the quantitization of Amlodipine and Olmesartan with many disadvantages over accuracy, precision, sensitivity, because zero order spectrums of drug substances are well affected by the interference of background matrix, surrounding environment. The reported method is irrelevant today, when there are many sophisticated techniques are available.

Unless and otherwise, the method is simple, convenient and be used when routine methods demand its application. The method employs methanol as the only solvent and no other reagent is required. The method utilizes very limited number of apparatus, i.e. routine laboratory glasswares used for dilutions purposes whereas the chromatographic techniques demand costly reagents, solvents and chemicals.