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OVERVIEW ON SPECTROPHOTOMETRIC AND CHROMATOGRAPHIC METHODS FOR ESTIMATION OF ATORVASTATIN CALCIUM AND SILDENAFIL IN BULK AND IN DIFFERENT DOSAGE FORMS

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ABSTRACT

Erectile dysfunction (ED) is a major health problem affecting 52% of men between 40 and 70 years. The association between ED and hypercholesterolaemia has also been studied extensively. Combination drug products occupy a time-honored and important role in therapeutics. The combination of Atorvastatin Calcium and Sildenafil is commercially available in tablet form to control erectile dysfunction. The Atorvastatin calcium and Sildenafil co- formulation, the IIEF-5 score was significantly decreased, maintaining cholesterol level. Analysis of samples with numerous components presents a major challenge in modern analysis. This article narrates different chromatographic (HPLC, HPTLC, UPLC, LC) & different spectrophotometric method (UV) for determination of the Atorvastatin Calcium and Sildenafil single drug as well as combination with other drug.

Keywords: Estimation, Atorvastatin Calcium, Sildenafil, UV Spectroscopy, RP HPLC

INTRODUCTION

Erectile dysfunction (ED) is a major health problem affecting 52% of men between 40 and 70 years **[1]**. The association between ED and hypercholesterolaemia has also been studied extensively **[2]**. Atorvastatin Calcium belongs to Statins class of drugs have common mechanism to inhibit cholesterol synthesis in the liver that involves blocking conversion of 3-hydroxy-3-methylglutharyl coenzyme A to mevalonate **[2, 3]**.

Sildenafil (SDF), 5-(2-ethoxy-5-((4-methylpiperazin-1-yl) sulfonyl)phenyl)- 1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d] pyrimidin-7- one, was the first oral medication approved by the US FDA for the management of ED. Pharmacologically, SDF enhances the ability of nitric oxide to inhibit Phosphodiesterase type 5 **[4, 5]**.

Combination drug products occupy a time-honored and important role in therapeutics. When rationally formulated, fixed-combination drugs may produce greater convenience, lower cost, and sometimes greater efficacy and safety **[6]**. Analysis of samples with numerous components presents a major challenge in modern analysis. Multi-component analysis has become one of the most appealing topics for analytical chemists in the last few years, in fields as clinical chemistry, drug analysis, pollution control **[7]**, etc.

The combination of ATC and SDF is commercially available in tablet form to control erectile dysfunction. The atorvastatin calcium and Sildenafil co- formulation, the IIEF-5 score was significantly decreased, maintaining cholesterol level. Both drugs were determined by spectrophotometry and HPLC methods **[8]**.

Different analytical techniques can be applied for multicomponent analysis including; Spectrophotometry, chromato-graphy, and electrophoresis **[9]**.

Different methods have been developed for determination of like UV-spectroscopy, liquid chromatography (HPTLC and HPLC) **[10]**.

Reported methods are categorized depending on the following considerations:

1. Single component analyzed by UV-spectroscopy methods and chromatographic method.
2. Analysis of Atorvastatin and Sildenafil from combination formulation by UV-spectroscopy methods and chromatographic method.

Table: 1 Analysis of Atorvastatin calcium from Analysis of single component & combination formulation by UV-Spectroscopy and Chromatographic methods

Sr. No	Drugs	Method	Description	Reference No.
1	Estimation of Atorvastatin Calcium in Tablet Dosage Form	UV Spectrophotometric	Detection wavelength: 246 nm in Methanol Linearity range: 5-25 µg/ml Co-relationCoefficient: 0.999. Absorption maxima: 10 µg/ml Recovery studies: 99.96%-100.03%	11
2	Estimation of Atorvastatin Calcium Form Tablet Dosage Forms	UV Spectrophotometric	Detection wavelength: 240 nm in 2.0 M urea solution Linearity range: 5-45 µg/ml Co-relationCoefficient: 0.999. LOD: 0.1025 LOQ: 0.3789	12
3	Development and Validation of a UV-Spectrophotometric Method for Quantification of Atorvastatin in Tablets	UV Spectrophotometric	Detection wavelength:248nm Solvent : Methanol: water (50:50) Linearity range: 5-15 µg/ml Absorption maxima : 10 µg/ml Recovery studies :98.78%-100.36%	13
4	Simultaneous estimation of Atorvastatin calcium and Clopidogrel Bisulphate in combined capsule dosage forms	Rp HPLC	Wavelength-245 nm Mobile Phase - Acetonitrile :0.1% orthophosphoric acid Mobile Phase ratio : 65: 35% v/v Stationary phase : Spherisorb, 5µ silica (4×250mm) column Sample Volume : 20µl Flow rate - 1ml/min Retention time -2.007 and 5.977min respectively Linearity range- 6 – 14 & 45 -105 µg/ml % RSD - 0.3775 ATR and 0.0411 for CLP.	14
5	Simultaneous estimation Atorvastatin calcium & Amlodipine Besylate in Bulk Pharmaceutical dosage form	Rp HPLC	Parameters for ATR &AML Wavelength-238 nm Linearity range- 5.0 – 50.0 & 2.5 -25 µg/ml Correlation co-efficient-0.999 1& 0.9988 LOD-0.076 & 0.088 LOQ-0.029 & 0.025	15
6	Simultaneous estimation Atorvastatin & Rosuvastatin in human serum	Rp-HPLC/UV	Wavelength-241nm Solvent-Methanol water Linearity range-2.0-256 ng/ml for rosuvastatin and 3.0-384ng/ml LOQ- Rosuvastatin 0.6 and 2.0 ng/ml while for Atorvastatin were 1.0 and 3.0ng/ml	16
7	Simultaneous estimation of Atorvastatin calcium and Felodipine in pure and combined capsule dosage form.	UV Spectrophotometric	Wavelength Atorvastatin-241nm Felodipin365.5 nm Solvent-Methnol Linearity range-2-10 µg/ml	17
8	Simultaneous estimation of Aspirin, Atorvastatin Calcium and Clopidogrel Bisulphate in Capsules	HPLC	Mobile Phase acetonitrile and 10 mmol/l potassium phosphate (50:50 v/v) Flow rate= 1.2 ml/min Wavelength-235 nm Linearity range- 30-105 & 5-30 µg/ml	18
9	Simultaneous estimation Atorvastatin calcium &	HPLC	Wavelength-361nm and 246 Linearity range- 0.5-30 µg/Ml	19

	Amlodipine Besylate in Tablet dosage forms.		**Recovery studies range from >99.82% for AMD and >98.09% for ATR**	
10	**Simultaneous estimation of Atorvastatin Calcium and Telmisartan Tablet dosage forms.**	**UV Spectrophotometric**	**Wavelength-219 nm and 257nm Linearity range- 50-150 mcg/ml and 10-50 mcg/mL Correlation co-efficient-0.9998 & 0.9999 %RSD < 2%**	**20**
11	**Simultaneous estimation of atorvastatin calcium and fenofibrate in tablet formulation**	**UV Spectrophotometric**	**Wavelength-245& 248nm Linearity range- 8-24 µg/ml, & 2-16 µg/ml for fenofibrate The recovery > 98%**	**21**
12	**Simultaneous estimation of Atorvastatin and Ezetimibe in tablet dosage form.**	**HPLC**	**Wavelength-233nm Linearity range- 5-25 µg/mL Retention time-3-5 & 4.4 min LOD (µg/ml)-0.06&0.062 LOQ (µg/ml)-0.2 & 0.211**	**22**
12	**Simultaneous estimation of Atorvastatin calcium (ATR) and Aspirin (ASP) in pure and combined capsule dosage form.**	**UV Spectrophotometric**	**Parameters for ASP&ATR Wavelength-222 & 242 nm Solvent-Methanol Linearity range-5-30 µg/ml & 5-40 µg/ml Correlation co-efficient-0.994& 0.996 LOD- 0.2582 & 0.3669 µg/ml LOQ- 0.4823 & 0.5337 µg/ml**	**23**

Table: 2 Analysis of Sildenafil from Analysis of single component & combination formulation by UV-Spectroscopy and Chromatographic methods

Sr.No	Drugs	Method	Description	Reference No.
13	**Detection of Sildenafil citrate in pure form and Pharmaceutical formulations.**	**UV Spectrophotometric**	**Wavelength- 228 nm Linearity Range- 10 to 50µg/ml Slope- 0.07877 Method Precision- % RSD 0.1175 Correlation Coefficient -0.9998**	**24**
14	**Sildenafil Citrate in pharmaceutical formulations.**	**RP-HPLC**	**Wavelength-230 Mobile Phase of Acetonitri le/Phosphate buffer (35:65, v/v) Retention time- 6.74±0.05. Linearity range 5-150µg/ml Flow rate - 1.0ml/m**	**25**
15	**Analysis of Sildenafil Citrate in pharmaceutical formulations.**	**RP-HPLC**	**Wavelength-228 Mobile Phase of-Acetonitrile/phosphate buffer) Mobile Phase Ratio- 70:30, v/v, Retention time- 4.087. Linearity range 0.1-30µg/ml Flow rate - 1.0ml/m**	**26**
17	**Determination of a binary mixture of TMD and SDF in rabbit plasma**	**HPLC-UV Spectrophotometric**	**MobilePhase -10 mM Na_2HPO_4 solution (pH 7.5): acetonitrile (45:55, v/v) Flow rate -0.8mL min−1 Wavelength-220nm Linearity range- 0.1-10 and 0.05-10 µg mL^{-1}**	**27**
18	**Simultaneous determination of Sildenafil citrate and Dapoxetine hydrochloride in a pharmaceutical formulation**	**UV Spectrophotometric**	**Sildenafil citrate and Dapoxetine Detection wavelength: 292& 231 nm Linearity 10 to 60 & 2–12 µg/mL Correlation coefficient -0.9991,0.9954 LOD : 0.5282mg/L,0.0904 mg/L LOQ : 1.6006mg/L 0.2741 mg/L**	**28**
19	**Simultaneous determination of**	**Stability indicating HPLC UV**	**Detection wavelength: 228nm Mobile Phase: Acetonitrile and 0.2M ammonium**	**29**

	sildenafil citrate and dapoxetine hydrochloride in Tablet		**acetate buffer Flow rate: 1.5mL/min Retention time: 3.392min and 7.255min linearity 5-180 and 1-40µg/mL Correlation coefficient -0.9999 and 0.9994**	
20	**Simultaneous determination of Sildenafil citrate and Dapoxetine hydrochloride in bulk and formulation**	**UPLC -MS/UV**	**Detection wavelength: 294 nm linearity 2.5-100 µg/ml LOD : 0.15-0.45 µg/ml LOQ : 0.1-0.3 µg/ml Stationary Phase: Acquity BEH Shield RP18 column**	**30**
21	**Simultaneous determination of Sildenafil citrate, Tadalafil and Vardenafil in formulation**	**High-temperature gas chromatography/mass spectrometry**	**Concentration ranges of 12.5–100 µg mg^{-1} for TD and VD, and 25–175 µg mg^{-1} for SD Recoveries were in the range of 87.3–102.4 %**	**31**
22	**Simultaneous determination of sildenafil citrate, Glimepiride in Rat Plasma**	**RP-HPLC**	**Detection wavelength: 230 nm Mobile Phase: methanol: water (85:15v/v) Retention time: Glimepiride 2.5 and sildenafil 4.0min Flow rate: 1.0ml/min**	**32**
23	**Simultaneous determination of Sildenafil citrate and Dapoxetine hydrochloride in a pharmaceutical formulation**	**UV Spectrophotometric**	**sildenafil citrate and dapoxetineHCl Detection wavelength sildenafil : 292 nm Dapoxetine: 231 nm Linearity range: sildenafil :2-20 µg/mL Dapoxetine: 1.2-12 µg/mL**	**33**
24	**Simultaneous determination of Sildenafil citrate and Dapoxetine hydrochloride in Tablet**	**Absorption Corrected**	**The amplitudes a-237.54 nm and 325.92 nm concentration range of 5-25 µg/ml for DPT and 8-40 µg/ml Flow rate: 1.0ml/min**	**34**
25	**Simultaneous determination of Sildenafil citrate, Tadalafil and Vardenafil in preparations and counterfeit drugs**	**RP-HPLC Method**	**Detection wavelength 230 nm Mobile Phase: 0.030 M of ammonium formate and Acetonitrile in the ratio 70:30 Retention times 1.654, 2.032, and 5.067 min for vardenafil, sildenafil, and tadalafil**	**35**
26	**Simultaneous determination of Moxifloxacin and Sildenafil citrate in a pharmaceutical Preparation**	**UV Spectrophotometric**	**Detection wavelength: Moxifloxacin 530 nm and Sildenafil 526 nm Linearity: Moxifloxacin 2.65 - 230.0 and Sildenafil 1.66 - 98.0 µg/mL LOD : Moxifloxacin 0.55 µg m/L, Sildenafil 0.44 µg/mL LOQ : Moxifloxacin 1.65 µg /mL Sildenafil 1.33 µg m/L Correlation coefficient: Moxifloxacin: 0.9999, Sildenafil : 0.9999 Mean % recovery ± SD: Moxifloxacin: 100.40 ± 0.16 Sildenafil : 100.12 ± 0.22**	**36**

CONCLUSION

This review summarized some of the reported Spectroscopic and Chromatographic methods developed and validated for estimation of Atorvastatin and Sildenafil. According to this review it was concluded that for Atorvastatin and Sildenafil different Spectroscopic and Chromatographic methods are available for single and combination also it was found that the mobile phase containing Methanol water, Acetonitrile, water, and 0.2M ammonium acetate buffer, Phosphate buffer were common for most of the chromatographic method to provide more resolution. It was observed that most common combination of Atorvastatin was with Clopidogrel Bisulphate and Sildenafil were with Dapoxetine. Finally we concluded that all methods found to be simple, accurate, economic, precise and reproducible in nature. Most of Methods were of RP-HPLC and UV absorbance detection because these methods provided with best available reliability, repeatability, analysis time and sensitivity.

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