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Reported estimation techniques for quantification of simvastatin: A review

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Abstract

Simvastatin is used along with a proper diet to help lower bad cholesterol and fats and raise good cholesterol in the blood. It belongs to a group of drugs known as statins. It works by reducing the amount of cholesterol made by the liver. Lowering bad cholesterol and triglycerides and raising good cholesterol decreases the risk of heart disease and helps prevent strokes and heart attacks. There are various analytical methods for estimation of the drug. This paper list outs the various analytical methods for the drug.

Keywords: Simvastatin; Antilipidemic agent; Analytical methods; Review

1. Introduction

Simvastatin is an HMG-CoA reductase inhibitor used to lower lipid levels and reduce the risk of cardiovascular events including myocardial infarction and stroke. Simvastatin is used to treat hypercholesterolemia. Its half-life is 2 hrs. The bioavailability of simvastatin is 5%. It is used along with exercise, diet and weight loss to decrease elevated lipid levels. It is also used to decrease the risk of heart problems in those at high risk. It is taken by oral route. It's molecular Formula $C_{25}H_{38}O_5$. Molecular weight 418.566g/mol, Pka value is in acidic-14.91, basic-2.8. It is practically insoluble in water freely soluble in chloroform, methanol and ethanol. Side effects are constipation, confusion, memory loss, nausea. The uses are to reduce risk of heart attack and stroke, to treat high cholesterol-NHS, it is used together with diet and weight loss. The structure of Simvastatin is in fig.1.

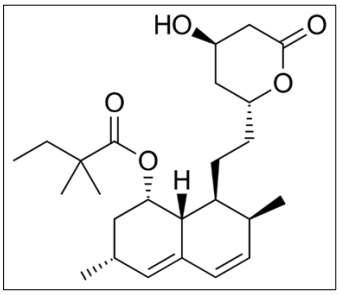

Figure 1 Structure of Simvastatin

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2. Various Analytical Methods

2.1. HPLC method

High-performance liquid chromatography (HPLC) methods for the determination of two major statins used in clinical treatment – simvastatin and atorvastatin – in various fields of application, including bio-analytical assays, pharmaceutical assays and environmental applications statin molecules are known to be susceptible to inter conversion of the lactone and acidic forms, so it is necessary to consider this phenomenon during method development. We highlight liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) methods, as they have become a method of choice in bio-analytical and environmental applications. We compare the methods from the point of view of sensitivity. We discuss selection of the precursor ion for performing selected reaction monitoring (SRM) in MS detection and sample preparation HPLC methods for the determination of simvastatin[1].

The aim of this study was to develop and validate a fast and simple reversed-phase HPLC method for simultaneous determination of four cardiovascular agents atorvastatin, simvastatin, telmisartan and irbesartan in bulk drugs and tablet oral dosage forms. The chromatographic separation was accomplished by using Symmetry C18 column (75 mm × 4.6 mm; 3.5 µ) with a mobile phase consisting of ammonium acetate buffer (10 mM; pH 4.0) and acetonitrile in a ratio 40:60 v/v. Flow rate was maintained at 1 mL/min up to 3.5 min, and then suddenly changed to 2 mL/min till the end of the run (7.5 min). The data was acquired using ultraviolet detector monitored at 220 nm. The method was validated for linearity, precision, accuracy and specificity. The developed method has shown excellent linearity ($R^2 > 0.999$) over the concentration range of 1-16 µg/mL. The limits of detection (LODs) and limits of quantification (LOQs) were in the range of 0.189–0.190 and 0.603–0.630 µg/mL, respectively. Inter-day and intra-day accuracy and precision data were recorded in the acceptable limits. The new method has successfully been applied for quantification of all four drugs in their tablet dosage forms with percent recovery within 100 ± 2%[2].

A simple, specific and sensitive reverse phase high performance liquid chromatographic method was developed and validated for simultaneous determination of ezetimibe and simvastatin from pharmaceutical dosage forms. The method uses C18 ODS Hypersil column and isocratic elution. The mobile phase composed of acetonitrile: phosphate buffer (pH 4.5, 0.01M) in the ratio of 65:35 v/v was used at a flow rate of 1.0 ml /min. UV detector was programmed at 232 nm for first 10 min and at 238 nm for 10 to 20 min. All the validation parameters were in acceptable range. The developed method was effectively applied to quantitate amount of ezetimibe and simvastatin from tablets. The method was also applied suitably for determining the degradation products of ezetimibe and simvastatin Stability Indicating RP-HPLC Method for Simultaneous Determination of Simvastatin and Ezetimibe from Tablet Dosage Form[3]

Statins are effective and often-prescribed drugs for the treatment of hypercholesterolemia. This study shows a simple and fast method validation by reversed-phase high-performance liquid chromatography in the linear range 28 to 52 µg/mL to quantify lovastatin, pravastatin sodium or simvastatin in bulk drug or dosage forms. Statins were determined using a C8 endcapped column (250 × 4 mm, 5 µm), isocratic mobile phase of acetonitrile and 0.1% phosphoric acid (65:35), 30 °C, ultraviolet–diode array detection at λ 238 nm and 1.5 mL/min flow for lovastatin and simvastatin and 1.0 mL/min for pravastatin sodium. The developed method is fast, simple, reliable and shows appropriate linearity ($r^2 > 0.999$), accuracy (98.8–101.6%), precision (relative standard deviation <2%) and selectivity toward placebo and/or degradation products in very similar chromatographic conditions for all statins[4].

To establish an RP-HPLC method for determination of simvastatin and its related substances. Chromatographic conditions were as followsa ZORBAX SB-C18 column(4.6 mm×250 mm, 5 µm) a mobile phase of CH_3CN -0.025 mol/L NaH_2PO_4 (65:35) a flow rate of 1.0 mL/min and a detection wavelength of 238 nm. Simvastatin and its related substances can be completely separated by the method with a liner range of 2-200 µg/mL. A detection limit of 5 ng/mL and a RSD of 3% were obtained. A reproducible and sensitive method is provided for determination of simvastatin and its related substances[5].

Sensitive, simple, reliable and rapid HPLC technique for the estimation of simvastatin (SMV) and cetirizine has been designed in this study. The chromatographic conditions were set using Shimadzu LC-10 AT VP pump, with UV detector (SPD-10 AV-VP). System integration was performed with CBM-102 (Bus Module). Partitioning of components was attained with pre-packed C-18 column of Purospher Star (5 µm, 250 x 4.6 mm) at ambient conditions. Injected volume of sample was 10 µl. Mobile phase was composed of 50:50 v/v ratio of Acetonitrile/water (pH 3.0 adjusted with ortho-phosphoric acid) having 2 ml/minutes rate of flow. Compounds were detected in UV region at 225 nm. Percent Recovery of simvastatin was observed in the range of 98-102%. All results were found in accept table range of specification. The projected method is consistent, specific, precise, and rapid, that can be employed to quantitate the SMV along with cetirizine HCl. It was estimated by 3 successive cycles of freeze and thaw stability. Results of FT samples were found

within accept table limits the method was developed and validated in raw materials, bulk formulations and final drug products. Estimation of simvastatin and cetirizine by RP-LC method: Application to freeze and thaw (FT) stability studies[6].

A simple, precise RP-HPLC method was developed for the estimation of ezetimibe and simvastatin in pure and pharmaceutical dosage forms. The quantification was carried out using a C-18 column 250 × 4.6 mm i.d., 5 µm particle size in isocratic mode, with mobile phase comprising of buffer and acetonitrile in the ratio of 45:55 (v/v) pH 7. The flow rate was 1 mL/min and the detection was carried out UV detector at 210 nm. The retention times were 12.06 and 18.97 min for ezetimibe and simvastatin, respectively. The method produced linear response in the concentration range of 25-125 µg/mL for ezetimibe and simvastatin. The percentage recovery was found to be 99.8 and 100% for ezetimibe and simvastatin, respectively. Atorvastatin used as an internal standard in the present study. The method validated by evaluation of required parameters. Validated Simultaneous Estimation of Simvastatin and Ezetimibe by RP-HPLC in Pure and Pharmaceutical Dosage Form[7].

A simple, rapid reverse phase high-performance liquid chromatographic method was developed and validated for the simultaneous estimation of Ezetimibe and Simvastatin in bulk and pharmaceutical dosage forms. Chromatography was carried out by using Chromosil C-18,column having 250 x 4.6mm internal diameter with a mixture of Methanol:Acetonitrile:0.1%Orthophosphoric Acid in the ratio of 75:20:05 (v/v/v) as mobile phase. Determination of the different analytical parameters such as linearity, precision, accuracy, and specificity, limit of detection (LOD) and limit of quantification (LOQ) was done. The calibration curve was found to be linear for each analyte in the desired concentration range. The average recovery was found to be 99.88 and 100.12 for Ezetimibe and Simvastatin respectively. The proposed method is highly sensitive, precise and accurate, which was evident from the LOD value of 1.2ppm and 0.25ppm for Ezetimibe and Simvastatin respectively and hence the present method can be applied successfully for the quantification of active pharmaceutical ingredient (API) content in the combined formulations of Ezetimibe and Simvastatin[8].

A simple, precise and rapid RP-HPLC method was developed for the simultaneous determination of simvastatin and ezetimibe in combined pharmaceutical dosage forms. The method was carried out on a Shim-pack, RP-C18 column using a mixture of acetonitrile: methanol: buffer (triethylamine pH-3) in the ratio 15:45:40 and detection was done at 240 nm using external standard method as quantitation. The linearity range of simvastatin and ezetimibe were 0.5 to 20 µg/ml. The intra-day and inter-day precision were in the range of 1.02-1.43 and 0.53-0.94 for simvastatin, 0.24-1.29 and 0.93-1.32 for ezetimibe[9].

Rapid reverse phase high-performance liquid chromatography (RP-HPLC) method was developed and validated for the simultaneous quantification of paracetamol, ibuprofen, olanzapine, simvastatin and simvastatin acid in the context of microalgae bioremediation. The method was validated according to the guidelines of the US Food and Drug Administration (FDA), the International Conference on Harmonization (ICH), and Eurachem with respect to system suitability, linearity, accuracy, precision, recovery, limits of detection and quantification, ruggedness, selectivity and specificity. The estimated limits of detection and quantification were, respectively, 0.03 and 0.10 µg/mL for paracetamol, 0.03 and 0.09 µg/mL for ibuprofen, 0.04 and 0.13 µg/mL for olanzapine, 0.27 and 0.83 µg/mL for simvastantin, and 0.05 and 0.14 µg/mL for simvastantin acid. The inter-day and intra-day precision results were within the acceptance limit of relative standard deviation (%RSD) of less than 2, and the percentage recovery was found to be within the required limits of 80–110%. The developed method is rapid, linear, precise, robust and accurate, and has been successfully applied to the determination of the above common pharmaceutical products during microalgae bioremediation[10].

A simple, precise and sensitive reverse-phase high performance liquid chromatographic method was developed and validated for the simultaneous determination of ezetimibe and simvastatin in pharmaceutical formulations. Chromatographic separation was performed on a Merck Cl 8 columnata wavelength of 240 nm using a mixture of 0.1M ammonium acetate buffer pH 5.0 and acetonitrile in the ratio of (30:70, v/v). The method results in excellent separation with good resolution between the two analytes. The within day variation was between 0.28 and 1.10 % and between day variation was between 0.56 and 1.32 %. The recovery was greater than 99.12 % with RSD less than 1.38 %. The method was validated according to ICH guidelines by performing linearity, accuracy, precision, limits of quantitation and selectivity. The results show mat the method is suitable for its intended use[11].

The aim of this study was to develop and validate a simple, rapid, precise, more accurate, reliable, least time consuming HPLC method for individual as well as simultaneous estimation of pravastatin, atorvastatin and simvastatin in bulk and pharmaceutical dosage form. The chromatographic separation was achieved by using a mixture of methanol and 0.1 % orthophosphoric acid in water as the mobile phase, with a C18 (150cm, 4.6 mm i.d., 2.7 µm) reversed-phase column at

flow rate of 1.0 mL/min and the eluents were monitered at 238 nm. A good linearity was found in the 0.12-0.24 mg/mL for both pravastatin and atorvastatin and 0.02-0.14 mg/mL simvastatin concentration range. The accuracy was good and recovery values for pravastatin, atorvastatin and simvastatin ranged from 99.21-100.40%, 99.87-100.39 and 98.84-100.66%, respectively. The proposed novel method was found to be efficient, accurate, precise, specific and economic and is suitable for individually as well as simultaneous estimation in quality control laboratories and research institutes[12].

2.2. UV Spectroscopy Methods

To develop two simple UV spectrophotometric methods for simultaneous estimation of Simvastatin (SMV) in bulk and tablet dosage form and validate as per ICH guidelines. Method A involved Absorbance maxima method which based on the measurement of absorbance of Simvastatin in methanol at Lambda max of Simvastatin 238 nm and Method B involved Area under the curve (AUC) method which based on the measurement of AUC in the range of 234-240 nm. The developed methods were validated for linearity, precision, accuracy, LOD and LOQ as per ICH guidelines. Both the methods were found to be linear within the conc. range of 4-32µg/ml for Simvastatin. The present methods were found to be simple, linear, precise, accurate and sensitive and can be used for routine quality control analysis for the estimation of Simvastatin in bulk and tablet dosage form[13].

An investigation of UV spectroscopic methods, i.e. absorbance, 1st and 2nd derivative spectra for the determination of simvastatin in tablet formulations has been undertaken. This work investigated the possible difficulties that might arise due to the presence of UV absorbing excipients and likely presence of degradation products in such assays. We have demonstrated that the presence of ascorbic acid as an excipient causes interference with simple absorbance measurements leading to a gross over- determination of the simvastatin. 1st and 2nd derivative methods appear to eliminate this problem. We have also shown that the degradation product of simvastatin, i.e. simvastatin-hydroxy acid, having an almost identical spectrum to the parent drug, may cause problems in the UV spectroscopic determination of the drug in degraded samples[14].

Simple accurate and precise spectrophotometric methods have been developed for the simultaneous estimation of simvastatin and sitagliptin by employing four different analytical UV-Spectroscopic methods. From them method A was simultaneous equation method involves formation and solving the simultaneous equation using 238 nm and 267 nm as two wavelengths for simvastatin and sitagliptin respectively. Method B related to first order derivative spectrophotometry. The first order derivative absorption at 230 nm was used for SIMV and 275nm was used. Method C is simultaneous estimation of simvastatin and sitagliptin by using dual-wavelength method. Method D involved in Q-absorption analysis based on the measurement of absorbance at two wavelengths that is the λmax of SITA 267 nm and iso -absorptive point of both drugs at 250 nm. Two wavelengths were selected for each drug in such a way that the difference in absorbance was zero for the second drug. At wavelengths 225 and 248 nm SITA had equal absorbance values; therefore, these two wavelengths have been used to determine SIMV; on a similar basis 254 and 274 nm were selected to determine SITA in their binary mixtures. The four methods were obeyed the Beer's law in the concentration range of 3-15 µg/ml for SIMV and 50-150 µg/ml for SITA. A new derivative and non-derivative UV-spectroscopic approach for quantification of simvastatin and sitagliptin in bulk and pharmaceutical formulation[15.]

A simple, accurate, precise, sensitive, and highly selective ultra violet spectrometer method has been developed for the simultaneous estimation of simvastatin and Metformin in bulk and solid dosage form. The estimation of simvastatin was carried out at 239 nm while metformin was estimated at 239 nm. The developed method was validated for linearity range, precision, recovery studies and interference study for mixture, all these parameter showed the adaptability of the method for the method quality analysis of the drug in bulk and combination formulation[16].

A new simple, precise spectrophotometric method was developed and validated for estimation of simvastatin from bulk and pharmaceutical formulation. In the present study, methanol as solvent and absorption maxima at 238 nm was used for estimation of simvastatin. The drug obeyed Beers law and showed good correlation. The linearity was observed between 2-18 µg/ml. The correlation coefficient was found to be 0.999. There was no significant difference in the precision analysis of simvastatin. The proposed method was validated statistically as per ICH guidelines with respect to recovery, linearity, Limit of detection (LOD) and Limit of quantitation (LOQ) and were found to be satisfactory. The method was developed and validated successfully for the quantitative validated UV spectrophotometric method for estimation of simvastatin in bulk and pharmaceutical formulation[17.]

Simple, accurate and precise spectroscopic method was developed for simultaneous estimation of ezetimibe and simvastatin in tablets using first order derivative zero-crossing method. Ezetimibe showed zero crossing point at 245.4 nm while simvastatin showed zero crossing point at 265.2 nm. The dA/dl was measured at 265.2 nm for ezetimibe and

245.4nm for simvastatin and calibration curves were plotted as dA/dl versus concentration, respectively. The method was found to be linear (r 2 >0.9994) in the range of 5-40 µg/ml for ezetimibe at 265.20 nm. The linear correlation was obtained (r 2 >0.9935) in the range of 5-80 µg/ml for simvastatin at 245.4 nm. The limit of determination was 0.39 and 0.12 µg/ml for ezetimibe and simvastatin, respectively. The limit of quantification was 1.10 and 0.4 µg/ml for ezetimibe and simvastatin, respectively. The method was successfully applied for simultaneous determination of ezetimibe and simvastatin in binary mixture[18].

A simple, accurate, precise, sensitive and a highly selective ultra violet spectrophotometric method has been developed for the simultaneous estimation of simvastatin and metformin hydrochloride in bulk and solid dosage form. The estimation of simvastatin was carried out at 247 nm while metformin hydrochloride was estimated at 232.2 nm. The developed method was validated for linearity, range, precision, recovery studies and interference study for mixture. All these parameters showed the adaptability of the method for the quality control analysis of the drug in bulk and in combination formulations[19].

Simple, accurate, precise, sensitive and selective spectrophotometric methods were developed for the estimation of simvastatin. The estimation of simvastatin was carried out by various solvents like ethanol (method I) at 238 nm, methanol (method II) at 235.8 nm and these methods were found to be linear in the range of 5-30µg/ml and 2-10 µg/ml of simvastatin for method I and II, respectively. The percent amounts of simvastatin estimated by method I and method II were found to be 99.12% and 98.94, respectively. The developed method was validated according to ICH guidelines and it found to be accurate and precise. Thus the proposed method can be successfully applied for simultaneous determination of simvastatin and in routine analysis work[20].

This research paper describes a simple, precise, and accurate UV-Vis Spectrophotometric method was developed and validated for simultaneous estimation of simvastatin (SIM) and fenofibrate (FEN) from their combination dosage form. This method includes the formation and solving of a simultaneous equation using 238 nm and 287 nm as two analytical wavelengths (λmax of the drugs) of detection. Both the drugs followed Beer-Lambert's law over the concentration range 0.60-3.60 µg/mL for simvastatin and 4.35-26.10 µg/mL for fenofibrate, respectively. Validation of the new developed method was done by linearity, precision, accuracy, limit of detection, limit of quantitation and robustness as per ICH guidelines and the results of the analysis were validated statistically. The available information from the research will be very informative towards the multi-component analysis of these drugs and will open new paradigms in the upcoming research in the field of analysis. Simultaneous estimation of simvastatin and fenofibrate from their combined dosage form by ultraviolet–visible spectroscopy using simultaneous equation method[21].

A simple, fast, and precise simultaneous spectrometric method for the estimation of Ezetimibe and Simvastatin in API and in synthetic mixture was developed. The proposed method is based on the formation and solving of simultaneous equations using 230 and 247.6nm as two analytical wavelength. Ezetimibe shows absortion maximum at 230nm and simvastatin shows absorbance at 247.6 nm in methanol. Beer's law was obeyed in the concentration range of 2-20µg/ml for Ezetimibe and 2-16 µg/ml for simvastatin. The molar absorptivity and sandell's sensitivity were found to be 1.703 $x10^4$ and 2.4 x 10^{-2} respectively for Ezetimibe and for simvastatin 2.23 x 10^4 and 1.87 x 10^{-2} respectively. The method allow rapid analysis of binary pharmaceutical formulation with accuracy. The results of analysis have been validated statistically and recovery studies confirmed the accuracy of the proposed method. The developed method was found to be very precise as % C.V calculated came out to be less than 2%. Simultaneous estimation of simvastatin by vierodt's method[22].

A simple, accurate and precise spectroscopic method was developed for simultaneous estimation of ezetimibe and simvastatin in tablets using first order derivative zero-crossing method. Ezetimibe showed zero crossing point at 245.4 nm while simvastatin showed zero crossing point at 265.2 nm. The dA/dl was measured at 265.2 nm for ezetimibe and 245.4nm for simvastatin and calibration curves were plotted as dA/dl versus concentration, respectively. The method was found to be linear (r 2 >0.9994) in the range of 5-40 µg/ml for ezetimibe at 265.20 nm. The linear correlation was obtained (r 2 >0.9935) in the range of 5-80 µg/ml for simvastatin at 245.4 nm. The limit of determination was 0.39 and 0.12 µg/ml for ezetimibe and simvastatin, respectively. The limit of quantification was 1.10 and 0.4 µg/ml for ezetimibe and simvastatin, respectively. The method was successfully applied for simultaneous determination of ezetimibe and simvastatin in binary mixture. Simultaneous spectroscopic estimation of ezetimibe and simvastatin in tablet dosage forms[23].

2.3. LC-MS-MS Methods

The Liquid Chromatography Tandem Mass Spectrometry (LC-MS-MS) for determination simvastatin in human plasma has been developed after extraction by ethyl acetate and hexane (90/10%, v/v) using lovastatin as internal standard.

The mobile phase consisting of mixture of acetonitrile and water (75/25%, v/v) 500µL/min by separated the solutes on a C18 column. The lower limit of quantitation of 0.25 ng/mL was achieved when the calibration curve was linear from 0.25-50 ng/mL. The entire run time for analysis was only 6 min. The quantitation in the selective reaction monitoring (SRM) in positive ion mode, the daughter ions m/z 325 for simvastatin and m/z 285 for lovastatin were used. The Parent ions in positive ion mode were m/z 441.3 for simvastatin and m/z 405.1 for lovastatin. The intra-day coefficients of variation were less than 14% while the inter-day coefficients of variation were less than 10%. The LC-MS-MS detection is sensitive due to its capability to eliminate interferences from endogenous components. Method Validation for Analysis of Simvastatin in Human Plasma Using Liquid Chromatography Tandem Mass Spectrometry (LC-MS-MS)[24].

Simvastatin acid (SSA, active metabolite of SS) and ezetimibe (EZM) in K2 EDTA containing human plasma, using simvastatin D6, simvastatin acid D3 and ezetimibe D4 as internal standards (ISTDs), respectively. A volume of plasma sample of only 400 µL was processed by the solid phase extraction technique; then 20 µL of processed sample was run on a Phenomenex, Kinetix XB C18, 150 × 4.6 mm, 5 µm column using an isocratic mobile phase consisting of 10 mM ammonium formate buffer (pH 4.0 ± 0.3): acetonitrile (27: 73, v/v) with a run time of 6.3 min. The precursor and product ions of SSA, EZM and their ISTDs were monitored on a triple quadrupole instrument operated in the negative ionization mode, and SS was monitored in the positive mode. The method was validated over a concentration range of 0.2–80 ng/mL for SS, 0.1–60 ng/mL for SSA and 0.05–15 ng/mL for EZM. The method has been successfully applied in clinical pharmacokinetic study in the Indian population. The Cmax, AUC0–inf and Tmax values obtained in our study were 10.61 ± 5.287, 77.58 ± 29.367 and 1.62 ± 0.436 for EZM; 69.74 ± 45.274, 190.71 ± 107.271 and 1.74 ± 0.480 for SS; and 25.36 ± 23.576, 139.24 ± 131.653 and 3.95 ± 0.671 for SSA, respectively. Development and Validation of an LC–MS-MS Method for the Simultaneous Determination of Simvastatin, Simvastatin Acid and Ezetimibe in Human Plasma and Its Application to Pharmacokinetic Study in the Indian Population [25].

A liquid chromatography–tandem mass spectrometry method was developed and validated for the simultaneous determination of simvastatin (SV) and simvastatin acid (SVA) in human plasma. To improve assay sensitivity and achieve simultaneous analysis, SVA monitored in (−)ESI (electrospray ionization) mode within the first 4.5 min and SV thereafter in (+)ESI mode. The separation of all compounds was achieved in about 6.2 min using a C18 reverse-phase fused-core column (Ascentis Express C18) and a mobile phase, which was composed of 2.00 ± 0.05 mM ammonium acetate buffer titrated to pH 3.8 with glacial acetic acid–acetonitrile (25:75, v/v), in isocratic mode at a flow rate of 0.500 mL/min. Additionally, a solid-phase extraction step was performed to reduce any ion-suppression and/or enhancement effects. The developed method was linear in the concentration range of 0.100–74.626 ng/mL for SV, and 0.100–48.971 ng/mL for SVA, with correlation coefficient greater than 0.99 for both analytes. The method has shown tremendous reproducibility, with intra- and inter-day precision <7.6%, and intra- and interday accuracy within ±10.9% of nominal values, for the both analytes. The method was successfully applied to characterize the pharmacokinetic profiles of SV and SVA following an oral administration of 40 mg SV tablet to healthy human volunteers. Development and Validation of an LC–MS-MS Method for Determination of Simvastatin and Simvastatin Acid in Human Plasma: Application to a Pharmacokinetic Study[26].

Three extraction methods were compared for their efficiency to analyze sitagliptin and simvastatin in rat plasma by LC–MS/MS, including (1) liquid–liquid extraction (LLE), (2) solid phase extraction (SPE) and (3) supported liquid extraction (SLE). Comparison of recoveries of analytes with different extraction methods revealed that SLE was the best extraction method. The detection was facilitated with ion trap-mass spectrometer by multiple reactions monitoring (MRM) in a positive ion mode with ESI. The transitions monitored were m/z 441.1→325.2 for simvastatin, 408.2→235.1 for sitagliptin and 278.1→260.1 for the IS. The lower limit of quantification (LLOQ) was 0.2 ng/mL for sitagliptin and 0.1 ng/mL for simvastatin. The effective SLE offers enhanced chromatographic selectivity, thus facilitating the potential utility of the method for routine analysis of biological samples along with pharmacokinetic studies. Comparison of conventional and supported liquid extraction methods for the determination of sitagliptin and simvastatin in rat plasma by LC–ESI–MS/MS[27].

2.4. Colorimetry Method

Complexing agent for improving drug solubility. The simvastatin complex with DMβCD was prepared using the co-evaporation method and was then characterized by differential scanning calorimetry (DSC), Fourier-transform infrared spectroscopy (FT-IR) and in vitro dissolution. Dissolution and pharmacokinetic studies indicated that the simvastatin/DMβCD complex exhibited an increased dissolution rate, rapid absorption, and improved bioavailability in rats compared to free drug. Maximum plasma concentration (cmax) and the time to reach it (tmax) were 21.86 µg/mL and 1.4 h for the drug complex, 8.25 µg/mL and 3.0 h for free drug, respectively. Main pharmacokinetic parameters such

as tmax, cmax were significantly different ($p < 0.01$) between the simvastatin complex and free drug. Bioavailability of the simvastatin complex relative to free drug was up to 167.0 %[28].

3. Conclusion

The collected methods are various analytical methods for the estimation of simvastatin. This is a non-lipid lowering drug. A few HPLC, LC-MS/MS methods have been for estimation simvastatin. UV and other analytical methods have been reported for the literature of estimation of simvastatin.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest.

References

[1] Lucie Nováková Dalibor Šatíns kýpetrsolic, TrAC Trends in Analytical Chemistry Volume 27, Issue 4April 2008, Pages 352-367

[2] Hassan A. Alhazmi, Mohmed N alnami, Mohammed A. A. Arishi, Sci. Pharm.Volume 86 Issue 110.3390/scipharm86010001.

[3] R. P. Dixit, C. R. Barhate, and M. S. Nagarsenker, Indian Journal of Pharmaceutical Sciences, 2022 | Vol 84 | Issue 4.

[4] Taízia D. SilvaMarcelo A. Oliveira, Renata B. de Oliveira, Journal of Chromatographic Science, Volume 50, Issue 9, October 2012, Pages 831–838,

[5] LIN, YingXIE, Jian-wei, XIE, Jian-wei Chinese Journal of Pharmaceutical Analysis Volume 25, Number 5, 1 May 2005, pp. 523-525(3)

[6] Khaled M. Alakhali, Journal of Clinical and Diagnostic Research, Issue November 2008, Volume 19(6), pages: 4303-4308.

[7] Safila Naveed, Khan Usmanghani, Aisha Sana, Huma Ali, January 2018 Pakistan Journal of Pharmaceutical Sciences 31(1):137-141.

[8] XIE, Hua1, ZHANG, Qiang1Qiang1, Chinese Journal of Pharmaceutical , nalysisVolume 25, Number 5, 1 May 2005, pp. 544-546(3).

[9] Krishnaveni, Department of Chemistry, K.B.N. College, Vijayawada, PVV, Sathyannarayana, Professor of Chemistry (Retired), ANU, Nagarjuna Nagar, International , Journal of Pharmaceutical and Life Sciences, Vol. 2 No. 5 (2013)2014-01-13

[10] Wencui Yin, Reem I. Al-Wabli, Adnan A. Kadi, Scientific Reports12, Article number: 4757 (2022) 01, 2020

[11] Ogun state Nigeria, Omeje Maxwell, Adewoyin Olusegun O. Joel Emmanuel S. Timothy Terhile Ang, Methodox, Volume 7, 2020.

[12] Usama A Fahmy, Journal of Chemical Pharmacetuical research Drug Design, Development and Therapy, Issue 2018, Volume 10, pages: 0975 - 7384

[13] Vinit Chavhan, Kavya Reddy, Kashmira Ahhirao, Estimation of Simvastatin in bulk and tablet dosage form Journal of Applied Pharmacy, Vol. 6 (2014) pages 255-265.

[14] J.S. Millership and J. Chin, From: Journal of Analytical Chemistry, Vol. 65, Issue 2.

[15] Rama Rao Nadendla, Abhinandana Patchala, International Journal of Botany Studies Vol. 6, Issue 2 (2021), Pages : 255-260

[16] Bulletin of Environment, Pharmacology and Life Sciences, Bull. Env. Pharmacol. Life Sci., Vol 9[7] June 2020 : 36-41

[17] Sandip A. Bandgar, Namdeo R. Jadhav, Estimation of Simvastatin in Bulk and pharmaceutical formulations , Research Journal of Pharmacy and Technology. Issue 2019; vol 12(12), pages 5745-5748.

[18] S. J. Rajput1 and H. A. Raj, Simultaneous spectroscopic estimation of ezetimibe and simvastatin in tablet dosage forms, Indian J Pharm Sci, 2007, 69 (6): 759-762

[19] Vineet Singla, Radhika Bhaskar and Rahul Bhaskar, Rasayan journal of chemistry Vol.3, No.3 (2010), 507-513

[20] Archana Sopan More, Bhushan Murlidhar Firake, Sandip Dinkar Firke, ACAIJ, 16(6) 2016 [258-264], Volume 16 Issue 6.

[21] Geeta Rajput, Saranjit Singh, Balak Das Kurmi, Journal armaspire 2021; Volume 13(1): pages117-121.

[22] Srivastava B., Akhtar J. and Baghel U.S. International Journal of Pharmacy and Life sciences, Issue June 2010, Volume: 1(2): 105-108 2005, pages 541-543(3).

[23] K Shivshanker, Dr. Nama Sreekanth, C Roosewelt, November 2007Asian Journal of Chemistry 19(6):4303-4308. 24.

[24] J. Chil, Muhammad Ashfaq, A Islam Ullahkhana, Syed Shanaz Qutabb, Syed Naeemrazzaqb, Journal of the Chilean Chemical Society, Chil. Chem. Soc, 52, 3 (2007) págs- 1220-1223

[25] Jiordanne Araújo Diniz, Davi da Silva Barbirato, Eduarda Helena Leandro doNasciment Andrea dos Anjos Pontual, Ana Cláudia Amorim Gomes Dourado , José Rodrigues Laureano Filho, Clinical Oral Investigations volume 26, pages3533–3545 (2022).

[26] Sathish Babu Munaga, Rajani Kumar Valluru, Phani Bhushana Reddy Bonga V. Sumathi Rao, Hemanth Kumar Sharma Journal of Chromatographic Science, Volume 54, Issue 6, July 2016, Pages 985–996.

[27] Pankaj Partani, Saurabh Manaswita Verma, Tausif Monif, Journal of Chromatographic Science, Volume 54, Issue 8, September 2016, Pages 1385–1396.

[28] Swati Gupta, Massimo Del Fabbro, Jia Cha, International Journal Implant Dentistry, Volume 5, Issue 1 June, 2018 ,pages 145-157.