

Comparative UV Spectral Study of Macitentan and Sildenafil in Tablet Formulations by UV-Visible Spectrophotometry

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ABSTRACT

Macitentan, a dual endothelin receptor antagonist, and Sildenafil, a phosphodiesterase-5 (PDE-5) inhibitor, are increasingly co-administered as combination pharmacotherapy for pulmonary arterial hypertension (PAH). Because a dedicated, comparative UV spectrophotometric profile for the two agents is not extensively documented, the present study was undertaken to characterise and compare their UV absorption behaviour under identical experimental conditions. Working solutions of Macitentan and Sildenafil (50 µg/mL in methanol) prepared from marketed tablet formulations were scanned individually over 200–400 nm using a UV-Visible spectrophotometer with methanol as blank. Macitentan showed a characteristic absorption maximum (λ_{max}) at 222 nm (absorbance 2.888), while Sildenafil showed λ_{max} at 228 nm (absorbance 3.420), a bathochromic shift of 6 nm. Sildenafil displayed a broader absorption range (200–358 nm; width 158 nm) than Macitentan (200–330 nm; width 130 nm), a wider full width at half maximum (48.5 nm vs. 31.8 nm), and approximately 18.4% higher absorbance intensity at its respective λ_{max} . Both drugs obeyed the Beer–Lambert law over 10–50 µg/mL, with Macitentan showing marginally superior linearity ($r = 0.9917$, $R^2 = 0.9835$) compared with Sildenafil ($r = 0.9760$, $R^2 = 0.9525$). The distinct spectral fingerprints obtained provide a scientific basis for selecting drug-specific analytical wavelengths and support the future development of a simple, rapid, and economical UV spectrophotometric method for the routine quality control of Macitentan–Sildenafil combination formulations.

Keywords: Macitentan, Sildenafil citrate, UV-Visible spectrophotometry, Comparative analysis, Method validation, ICH guidelines, Tablet formulation

INTRODUCTION

Pharmaceutical analysis forms the scientific backbone of drug development, manufacturing, and quality control, encompassing the identification, characterisation, and quantitative determination of the chemical constituents of drug substances and products. With combination pharmacotherapy — in which two or more active pharmaceutical ingredients (APIs) are formulated or co-administered to achieve synergistic or complementary therapeutic action — becoming increasingly common, regulatory bodies such as the US FDA, the International Council for Harmonisation (ICH), and national pharmacopoeial commissions mandate rigorous quality-control testing of every drug product prior to release. Among the analytical techniques available, UV-Visible (UV-Vis) spectrophotometry continues to occupy a position of importance because of its simplicity, sensitivity, cost-effectiveness, wide availability, and minimal sample-preparation requirements.

UV-Vis spectrophotometry is an absorption technique that measures the extent to which a chemical species in solution absorbs ultraviolet (190–400 nm) or visible (400–800 nm) radiation. Absorption arises from electronic transitions ($\sigma \rightarrow \sigma^*$, $n \rightarrow \sigma^*$, $\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$) within molecules possessing chromophoric groups such as aromatic rings, conjugated double bonds, or heteroatoms bearing lone-pair electrons; auxochromes ($-\text{OH}$, $-\text{NH}_2$, $-\text{OCH}_3$, $-\text{SH}$) further modify the intensity or position of absorption. Because a very large proportion of drug molecules possess such chromophores, UV spectrophotometry remains the technique of first choice for routine quality control in resource-limited academic and small-scale industrial laboratories, obviating the need for the expensive columns, mobile phases, and long run times associated with chromatographic methods.

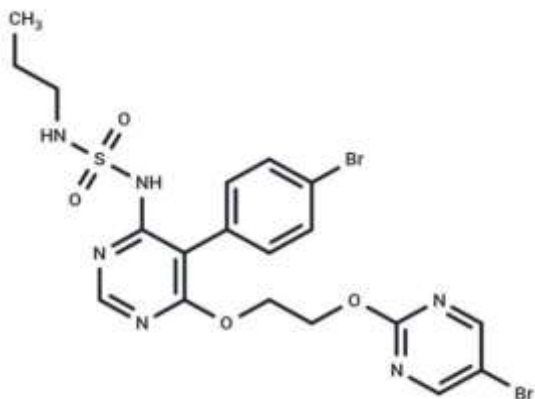


Fig. no.1 Structure of macitentan

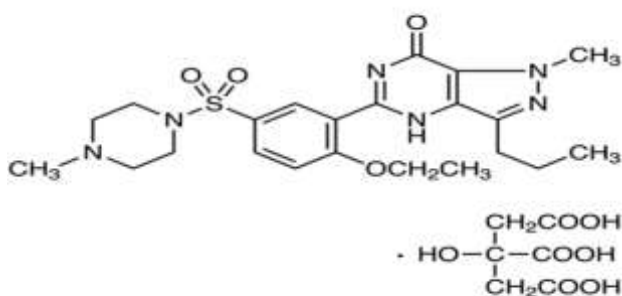


Fig.no.2 Structure of sildenafil citrate

MATERIALS AND METHODS

Chemicals and reagents

Marketed tablet formulations of macitentan (*Macitent*, 10mg) and sildenafil citrate (*Zenegra*, 50mg) were procured from the local pharmacy. Analytical reagent (AR)/HPLC grade methanol and other reagents were procured from *SiVerce Solutions (OPC) Private Limited., Bengaluru, India*.

Instrumentation

A double-beam UV-Visible spectrophotometer (Model: *GENESYS 180*) with matched 1 cm quartz cells was used for all spectral and absorbance measurements. An electronic analytical balance, ultrasonic bath sonicator, and calibrated volumetric glassware were used throughout the study.

Preparation of sample solution

Macitentan, ten tablets (10 mg each) were weighed and finely powdered; powder equivalent to one tablet (≈ 0.072 g) was transferred to a 100 mL volumetric flask, extracted with ≈ 70 mL methanol by sonication (15 min), made up to volume, and filtered (Whatman No. 41) to give a 100 $\mu\text{g/mL}$ stock solution. A 5 mL aliquot was diluted to 10 mL with methanol to obtain a 50 $\mu\text{g/mL}$ working solution.

Sildenafil, ten tablets (50 mg each) were weighed and powdered; powder equivalent to one tablet (≈ 0.240 g) was extracted in the same manner to give a 500 $\mu\text{g/mL}$ stock solution, from which a 1 mL aliquot was diluted to 10 mL with methanol to obtain a 50 $\mu\text{g/mL}$ working solution. Methanol served as the blank in all measurements, with baseline correction performed over 200–400 nm before sample analysis.

UV spectral scanning and linearity

The 50 µg/mL working solutions of each drug were scanned individually against methanol (200–400 nm; 10 mm quartz cuvette) under identical instrumental conditions, and λ_{max} , absorbance, peak shape, and spectral profile were recorded. Spectra were overlaid to compare λ_{max} , peak intensity, peak symmetry, and spectral overlap. For the linearity study, five concentrations (10–50 µg/mL) of each drug were prepared and their absorbance recorded at the respective λ_{max} ; the resulting data were fitted by linear regression ($y = mx + c$).

Determination of λ_{max}

Sample of macitentan and sildenafil citrate were scanned separately in the UV range of 200–400 nm against the solvent blank to determine the wavelength of maximum absorption (λ_{max}) for each drug. The wavelength showing maximum and reproducible absorbance was selected for subsequent quantitative measurements. macitentan as Characteristic λ_{max} absorption wavelength at **222nm** and sildenafil as Characteristic λ_{max} absorption wavelength at **228nm**

Construction of calibration curve

Aliquots of the working solutions were diluted appropriately to obtain a series of concentrations in the range of [10–50 µg/mL] for each drug. The absorbance of each solution was measured at the respective λ_{max} against the solvent blank, and calibration curves were plotted as absorbance versus concentration.

Assay of marketed tablet formulations

Twenty tablets of each formulation were weighed and finely powdered. A quantity of powder equivalent to one average tablet weight (containing a known amount of drug) was accurately weighed, dissolved in the solvent, sonicated for 15 minutes to ensure complete extraction, filtered through Whatman filter paper No. 41, and diluted appropriately to obtain a solution within the linearity range. The absorbance was measured at the respective λ_{max} , and the amount of drug present was computed using the corresponding regression equation.

RESULTS

The overlain UV absorption spectra of macitentan and sildenafil citrate

Wavelength of maximum absorption (λ_{max})

The λ_{max} is the most diagnostic spectral parameter of a compound, being unique to its molecular structure and chromophoric composition. Under identical experimental conditions, Macitentan showed a characteristic λ_{max} at 222 nm, while Sildenafil showed λ_{max} at 228 nm — a difference of 6 nm. This bathochromic (red) shift for Sildenafil relative to Macitentan suggests a somewhat greater degree of electronic conjugation in the Sildenafil chromophore, permitting absorption of lower-energy (longer-wavelength) UV radiation.

Table 1: wavelength of λ_{max}

parameter	Macitentan	Sildenafil
Scan range	200–400	200–400
Characteristic λ_{max}	222 nm	228 nm
Absorbance at λ_{max}	2.888	3.420
$\Delta\lambda_{\text{max}}$ (Sildenafil – Macitentan)	6 nm	

Table 2: Absorbance intensity at λ_{max}

Parameter	Macitentan	Sildenafil	Interpretation
λ_{max}	222nm	228nm	Sildenafil absorbs at a longer wavelength
Maximum absorbance	2.888	3.420	Sildenafil shows stronger UV absorption
Difference in absorbance	-	0.352AU	Sildenafil absorbs 0.352 AU more
Absorbance ratio	1.00	1.18	Sildenafil is 1.18-fold higher
Percentage difference	-	18.24%	Sildenafil is ~18% more intense

Table 3: Absorption range

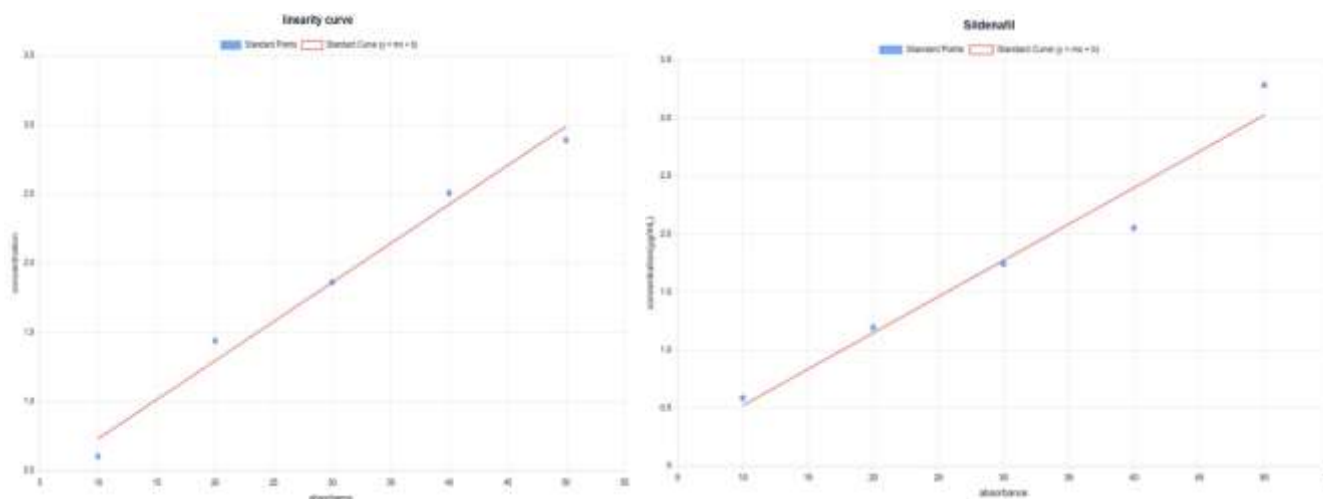
Parameter	Macitentan	Sildenafil	Comparison
Absorption range	200–330 nm	200–330 nm	Sildenafil wider
Starting wavelength	200 nm	200 nm	Similar
Ending wavelength	330 nm	358 nm	Sildenafil +28 nm
Range width	130 nm	158 nm	Sildenafil wider by 28 nm
% wider (Sildenafil vs Macitentan)	-	21.53%	-

Table 4: spectral shape (peak profile)

parameter	Macitentan	Sildenafil
Main λ_{max}	222 nm	228nm
Amax (AU)	2.888	3.240
FWHM	31.8	48.5
Peak type	Broad	Board
Peak symmetry	Asymmetric	Asymmetric
Secondary peak	present	Present
Shoulder	absent	Absent

Table 5: Linearity and conformity with Beer–Lambert's law

Concentration ($\mu\text{g/mL}$)	Absorbance — Macitentan (222 nm)	Absorbance — Sildenafil (228 nm)
10	0.603	0.587
20	1.439	1.193
30	1.861	1.743
40	2.507	2.053
50	2.890	3.285



Regression analysis gave $y = 0.0564x + 0.1673$ ($r = 0.9917$; $R^2 = 0.9835$) for Macitentan and $y = 0.0625x - 0.1037$ ($r = 0.9760$; $R^2 = 0.9525$) for Sildenafil. Both correlation coefficients indicate good linearity over the studied range, with Macitentan showing marginally superior linearity than Sildenafil under the present conditions.

parameter	Macitentan	Sildenafil	Comparison
Concentration range	10–50 $\mu\text{g/mL}$	10–50 $\mu\text{g/mL}$	Same
λ_{max}	222 nm	228 nm	Different
Slope (m)	0.0564	0.0625	Sildenafil higher
Intercept (c)	0.1673	–0.1037	Different
Correlation coefficient (r)	0.9917	0.9760	macitentan
R^2	0.9835	0.9525	Macitentan higher
Linearity	Good	Moderate–good	Macitentan better

DISCUSSION

Taken together, the results show that Macitentan and Sildenafil are spectrally distinguishable despite both being administered together in PAH management. The 6 nm bathochromic shift, the 0.352 AU (18.4%) higher absorbance, the 16.7 nm broader FWHM, and the 28 nm wider absorption range observed for Sildenafil relative to Macitentan collectively reflect the greater electronic conjugation of its pyrazolopyrimidinone-sulfonamide chromophore compared with the bromophenyl-bromopyrimidine system of Macitentan. Because the two drugs' λ_{max} values are only 6 nm apart and their absorption ranges overlap substantially between 210–300 nm, simple single-wavelength UV assay of one drug in the presence of the other would be subject to mutual spectral interference; simultaneous- or derivative-spectrophotometric approaches, or prior chromatographic separation, would therefore be required for a combined-formulation assay. Nonetheless, the distinct λ_{max} , peak width, and linearity behaviour identified here provide a sound basis for selecting drug-specific analytical wavelengths (222 nm for Macitentan; 228 nm for Sildenafil) for their independent

estimation, and for the future design of a validated simultaneous-equation or derivative UV method, in accordance with ICH Q2(R1)/Q2(R2) guidelines, for combination tablet formulations.

CONCLUSION

A comparative UV spectrophotometric study of Macitentan and Sildenafil in tablet formulations was carried out under identical experimental conditions using methanol as solvent. The two drugs showed clearly distinguishable UV absorption profiles: Macitentan exhibited λ_{max} at 222 nm with narrower and less intense absorption, while Sildenafil exhibited λ_{max} at 228 nm with a broader, more intense, and more extended absorption profile. Both drugs obeyed the Beer–Lambert law over 10–50 $\mu\text{g/mL}$, confirming the applicability of UV spectrophotometry for their quantitative estimation. These findings establish a scientific basis for the selection of analytical wavelengths and support the future development of a simple, rapid, precise, and economical UV spectrophotometric method for the routine quality control — including assay, content uniformity, and dissolution testing — of Macitentan and Sildenafil, individually or as combination formulations, in academic and small- to medium-scale pharmaceutical quality-control laboratories.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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AUTHOR CONTRIBUTIONS

Author 1: conceptualization, experimental work, data analysis, manuscript drafting, supervision, review and editing, final approval

AI USE STATEMENT

The author(s) used an AI-assisted tool (Claude, Anthropic) for formatting this manuscript into the journal's prescribed template structure. The author(s) reviewed, verified, and take full responsibility for the accuracy and authenticity of all scientific content, data, and conclusions presented in this manuscript.

REFERENCES

- 1) International Conference on Harmonisation (ICH). Q2(R1): Validation of Analytical Procedures: Text and Methodology. Geneva: ICH; 2005.
- 2) US Food and Drug Administration. Opsumit (macitentan) tablets: prescribing information. Silver Spring (MD): FDA; 2013.
- 3) US Food and Drug Administration. Revatio (sildenafil) tablets: prescribing information. Silver Spring (MD): FDA; 2005.
- 4) Patil DR, Neve TD. Development and Validation of UV-Spectrophotometric Method for Macitentan Bulk Drug and Formulation. *International Journal of Pharma Research and Technology*. 2022;1(1):1–7.

- 5) Kocak OF. A New Spectrophotometric Method for the Determination of Macitentan in Human Plasma. *Natural Products and Biotechnology*. 2022;2(2):74–80.
- 6) Lakka NS, Kuppan C, Rangasamy P. Impurity profile of macitentan in tablet dosage form using a stability-indicating high performance liquid chromatography method and forced degradation study. *Journal of Pharmaceutical Analysis*. 2019. doi:10.3724/SP.J.1123.2018.06032.
- 7) Sabbani Ranjith Kumar M. Analytical Method Development and Validation of Macitentan and Tadalafil Using RP-HPLC in Bulk and Tablet Formulations. *World Journal of Pharmaceutical Sciences*. 2025;13(3).
- 8) Lusina M, et al. Analytical approaches for the determination of endothelin receptor antagonists in pharmaceutical formulations. *Journal of Pharmaceutical and Biomedical Analysis*.
- 9) Kocak OF, et al. Analytical determination of endothelin receptor antagonist drugs using spectrophotometric approaches. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*.
- 10) Katsuki Y, et al. Analytical investigation of macitentan and its related substances in pharmaceutical formulations. *Journal of Pharmaceutical Sciences*.
- 11) Iglarz M, Binkert C, Morrison K, et al. Pharmacology of macitentan, a tissue-targeting endothelin receptor antagonist. *Journal of Pharmacology and Experimental Therapeutics*. 2011;339(2):658–665.
- 12) Sidharta PN, van Giersbergen PLM, Halabi A, Dingemanse J. Macitentan: entry-into-human study with a new endothelin receptor antagonist. *European Journal of Clinical Pharmacology*. 2011;67:977–984.
- 13) Dingemanse J, Sidharta PN, Madduri RP, et al. Clinical pharmacology and pharmacokinetics of macitentan. *Clinical Pharmacokinetics*.
- 14) Iglarz M, Binkert C, Gellert L, et al. Pharmacological characterization of macitentan and its active metabolite in endothelin receptor assays. *Journal of Pharmacology and Experimental Therapeutics*.
- 15) Pulido T, Adzerikho I, Channick RN, et al. Macitentan and morbidity and mortality in pulmonary arterial hypertension. *New England Journal of Medicine*. 2013;369:809–818.
- 16) Vidya Sagar G. Spectrophotometric Determination of Sildenafil in Tablets. *Asian Journal of Chemistry*. 2004;16(3):1435–1438.
- 17) Silva TD, Toledo CR, Vianna-Soares CD. Development and validation of alternative methods by non-aqueous acid-base titration and derivative ultraviolet spectrophotometry for quantification of sildenafil in raw material and tablets. *Brazilian Journal of Pharmaceutical Sciences*. 2017;53(1):e15181. doi:10.1590/S2175-97902017000115181.
- 18) Mohammed AAW, Mohammed SE, Boshra HS, Abdelmula MH. Development and Validation Method for the Determination of Sildenafil Citrate Tablets by Using UV-Spectrophotometer in Pharmaceutical Formulation. *Biotechnology: An Indian Journal*. 2019;15(2):182.