UNIVERSAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH (UJPSR)
Volume 10 Issue 1 Year 2026 Page No. 39 – 44
Estd. 1990

Derivative spectrophotometric method with greenness assessment for the simultaneous determination of naproxen and domperidone

Arnab Rakshit, Usha Khanal, Nihar Ranjan Bhuyan, Bhupendra Shrestha, Dawmit Lepcha*
Department of Pharmaceutical Analysis, Himalayan Pharmacy Institute, Majitar, Sikkim - 737136

Article History
Received : 17th March 2026
Revised : 14th May 2026
Accepted : 20th May 2026
Published : 30th June 2026

Keywords
Naproxen, Domperidone, Zero-crossing point, first-order derivative, spectrophotometric

Abstract
A simple and accurate first-order derivative UV spectroscopy method was developed for simultaneous estimation of Naproxen and Domperidone. The method resolves spectral overlap using 255 nm for Domperidone and 283.5 nm for Naproxen. Linearity was performed in the range of 5–100 µg/mL for Naproxen and 1–100 µg/mL for Domperidone, with correlation coefficients (R^2) of 0.999 and 0.998, respectively. Precision studies show low %RSD values (<1.5%), and recovery ranged from 97.91% to 102.39% for Naproxen and 99.33% to 101.25% for Domperidone, complying the method's accuracy and reproducibility. The limits of detection and quantification were found to be 1.09 and 3.30 µg/mL for Naproxen and 1.096 and 3.32 µg/mL for Domperidone. Greenness assessment was carried out using Analytical Eco-Scale (score: 80), Green analytical procedure index (68), Blue analytical grade index (67.5), and Analytical GREEness matric approach (0.48). The method is sensitive, reliable, and moderately green for routine analysis of Naproxen and Domperidone.

INTRODUCTION

Naproxen (NAP) is (2S)-2-(6-methoxynaphthalen-2-yl) propionic acid (fig.1) is one type of NSAID which effectively reduce pain, inflammation and fever(1). Being non-selective, it works by blocking the activity of cyclooxygenase enzyme (COX-1 and COX-2)(2,3). However it causes side effect as a gastrointestinal irritation, nausea, vomiting(4). Domperidone (DOM) is 5-chloro-1-[1-[3-(2-oxo-2,3-dihydro-1H-benzimidazol-1-ylpropyl]piperidin-4-yl]-1,3-dihydro- 2H-benzimidazol-2-one, (fig.2)(3). Domperidone's antiemetic and antinauseant properties make it one of the most commonly used medications(5). It is used to alleviate nausea and vomiting. Additionally, it also enhances food passage through the stomach by increasing motility of intestinal tract and stomach(6). Domperidone induced migraine-related nausea and vomiting(7). A unique combination of Naproxen 500mg and Domperidone 10mg are readily available in the Indian market where, Naproxen is used to relieve migraine on the other hand, Domperidone act as a dopamine receptor antagonist (8). It blocks the dopamine receptors present at

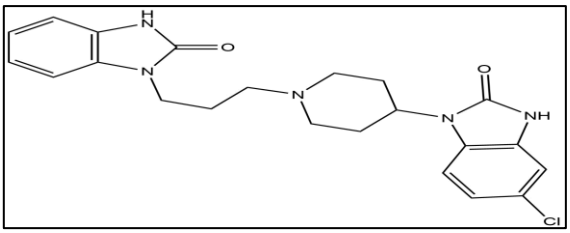

Fig 1 Naproxen

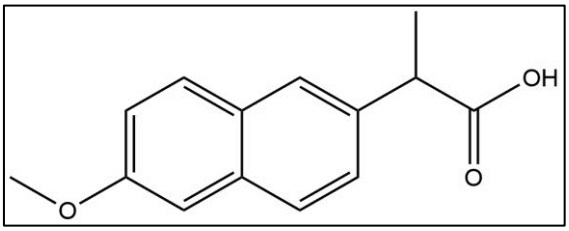

Fig 2 Domepridone

the chemoreceptor trigger zone which is responsible for regulating nausea and vomiting (9). Combination of these two drugs is available in the market named as - Naxdom, Napra-D, Naprozen etc.

In the review of literature, several spectrophotometric and chromatographic methods have been reported for the estimation of Naproxen and Domperidone, both in combination and with other drugs like RP-HPLC method

For correspondence: subbamanjeela@gmail.com

(10), HPLC method and UV Spectrophotometry (11,12). Simultaneous estimation of Naproxen and Domperidone using UV spectrophotometry and various spectrophotometric methods such as isoabsorptive point, ratio subtraction, ratio difference, and mean centering have been described (13,14). Other reported methods include the determination of Domperidone in tablet formulation, and in combination by RP-HPL (15,16) and the estimation of Naproxen using UV spectroscopy and RP-HPLC techniques (17). Despite extensive studies, an official method for the simultaneous determination of NAP and DOM in combined dosage form using the first-order derivative approach has not been established in the literature. The Derivative spectrophotometry offers two main objectives. Firstly, it enhances the resolution of overlapping bands, allowing for more accurate detection of individual maxima. Secondly, it prefers substances with narrow spectral bandwidths (18). Since Domperidone and Naproxen meet this criterion, therefore derivative spectrophotometric method with zero crossing technique is used for their analysis in this study.

Hence, a simple, selective, and reliable first-order derivative spectrophotometric method was developed for the simultaneous determination of Naproxen and Domperidone in tablet dosage form. Along with analytical performance, attention was also given to the method's environmental impact, in line with the growing emphasis on green analytical chemistry(19). Traditional approach often involves toxic solvents and generate hazardous waste, raising concerns about health, environmental safety, and regulatory compliance. To ensure the method aligns with sustainability principles, various greenness assessment tools were employed. The Green Analytical Procedure Index (GAPI) provided a step-by-step visual assessment of the method's ecological profile using a color-coded pictogram(19,20), while the Blue Analytical Greenness Index (BAGI) evaluated practical aspects based on ten parameters shown in a blue-shaded diagram(21) . The Analytical Eco-Scale offered a semi-quantitative score by deducting penalty points from a baseline of 100, accounting for reagent toxicity, waste, and energy consumption(22,23) . Furthermore, the Analytical GREEnness Metric Approach (AGREE tool) summarized the method's adherence to all 12 green analytical chemistry principles into a single circular pictogram with a composite score from 0 to 1, with higher scores indicating greener methods (24,25).

MATERIALS AND METHODS

A UV spectrophotometer (Shimadzu UV-1800) equipped with two matched quartz cells of 1 cm path length was used for recording spectra and measuring absorbance. The instrument was operated using UV Probe software (version 2.4.1). An analytical balance (Sartorius CP225D) was used for all weighing procedures, and an ultrasonic bath sonicator (Optics Technology) was employed for the sonication of analytical solutions. Pure samples of Naproxen and Domperidone were obtained as gifted samples from MacLeods Pharmaceutical Ltd. Sikkim. The tablet formulation Naxdom, containing 500 mg of Naproxen and 10 mg of Domperidone (Batch No. FHC0312), was purchased from the local market and is manufactured by Sun Pharmaceutical Industries Ltd., India. Distilled water was used for all studies.

PREPARATION OF STANDARD STOCK SOLUTION

A standard stock solution of DOM and NAP were prepared separately by transferring accurately 10.0 mg of drug powder into a clean and dry 10.0 ml volumetric flask and dissolved in a 5.0 ml methanol and rest of 0.1N NaOH. Final Concentration was 1000 µg/ml.

Further dilutions of the stock solutions were prepared using 0.1 N NaOH to obtain working standard solutions within the desired concentration range

PREPARATION OF WORKING STANDARD SOLUTION

From the standard stock solution 6 working standard solutions having concentration 100, 50, 25, 20, 2.5, 1 µg/ml for

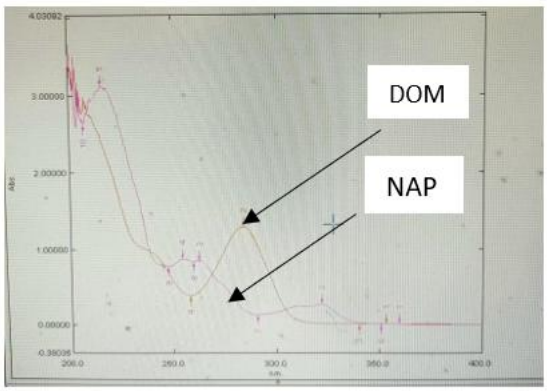

FIG 3. Spectra of Naproxen and Domperidone at 100µg/ml

Domperidone and 100, 50, 25, 20, 10, 5 µg/ml for Naproxen were prepared separately using 0.1 N NaOH. and were scanned in the wavelength range of 200-400 nm and the overlain spectra was obtained using UV- Probe software (fig.3).

SELECTION OF WAVELENGTH

The absorption spectra obtained were derivatized for both the standard (NAP and DOM). First order derivative spectra was selected for both the standard having two zero

crossing points at wavelength of 255 nm and 283.5nm for NAP and DOM respectively (fig 4). Further the wavelength of 255nm identified as the zero crossing point of NAP, was used for the analysis of DOM, similarly the wavelength 283.5 nm was used to analyze the NAP.

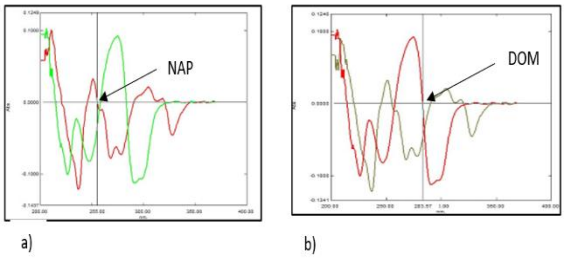

FIG 4. Overlay Spectra of Naproxen and Domperidone at 100µg/ml. a) Zero crossing point of NAP and b) zero crossing point of DOM.

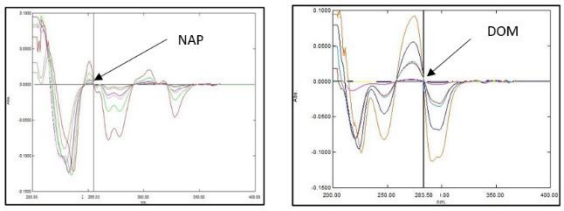

FIG 5. Zero crossing points for different concentration of NAP and DOM

PREPARATION OF SAMPLE SOLUTION

Twenty Naxdom 500 tablets were accurately weighed and finely powdered. From the resulting powder, a portion equivalent to 50.0 mg of tablet powder, containing approximately 49.0 mg of Naproxen and 1.0 mg of Domperidone, was transferred to a 100.0 mL volumetric flask. It was dissolved in 5.0 mL of methanol, and the volume was made up to the mark with 0.1 N NaOH. The resulting solution was then filtered using Whatman No. 1 filter paper. From the filtrate, approximately 1.0 mL was pipetted and further diluted to 10.0 mL with 0.1 N NaOH. Standard solutions containing 10 µg/mL of DOM were individually prepared by suitably diluting the standard stock solution, and this standard was then added to the sample preparation. The final sample solution were measured in quantitation derivative mode to obtain 1st order absorbance in 1 cm cell against solvent blank with absorbance values recorded at 255 nm and 283.5 nm.

METHOD VALIDATION PARAMETERS

LINEARITY

LINEARITY OF NAP

A stock solution of Naproxen was prepared by accurately weighing 10.0 mg of the drug and transferring it into a 10.0 mL volumetric flask. The drug was dissolved in 5.0 mL of methanol, shaken thoroughly, and the volume was adjusted to the mark with 0.1 N NaOH. From this stock, a series of standard solutions with concentrations ranging from 5 to 100 µg/mL were prepared using 0.1 N NaOH. Absorbance values were measured at 283.5 nm, and a calibration curve was constructed by plotting absorbance against concentration. The regression equation and correlation coefficient (R^2) were determined from the curve.

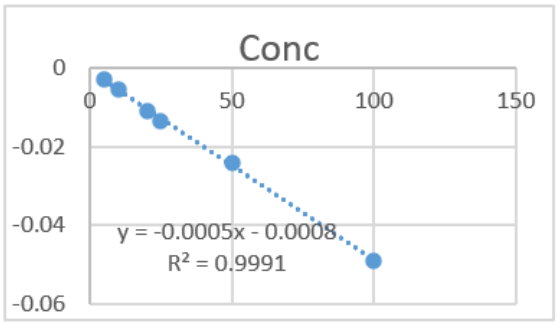

Fig 6: Std. calibration curve of Naproxen

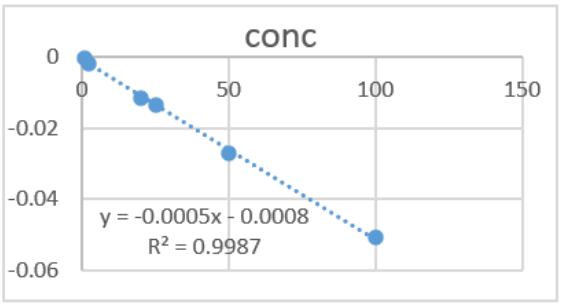

Fig 7: Std. calibration curve of Domperidone

PRECISION

Method precision was evaluated through intra-day and inter-day studies. A synthetic mixture weighing 92.2 mg, equivalent to 50.0 mg of NAP, was prepared along with 10.0 mg of DOM. The contents were dissolved in 5 mL methanol and the volume was made up to 100.0 mL with 0.1 N NaOH. From this, a solution containing 50 µg/mL of NAP and 1 µg/mL of DOM was prepared and analyzed six times under identical conditions. The absorbance was recorded for each replicate, and the mean, standard deviation (SD), and relative standard deviation (%RSD) were calculated to evaluate method precision.

ACCURACY

Known quantities of pure Naproxen and Domperidone standards were added to previously analyzed tablet samples at three concentration levels—80%, 100%, and 120% of the nominal value. Each level was tested in triplicate.

The percentage recovery was determined using the formula:

Accuracy = (found- nominal) / nominal x 100

LIMIT OF DETECTION AND LIMIT OF QUANTIFICATION (LOD & LOQ)

The LOD and LOQ were calculated based on the standard deviation of the response (σ) and the slope (S) of the calibration curve, using the following equations:

$LOD = 3.3 \times (\sigma / S)$

$LOQ = 10 \times (\sigma / S)$

Where,

σ = the standard deviation of the responses

S = the slope of calibration curve.

Solutions in the concentration range of 5–100 µg/mL for NAP and 1–100 µg/mL for DOM were used to obtain the calibration curve. The standard deviation of the response was calculated using Microsoft Excel, and the slope was derived from the linear regression equation.

RESULTS AND DISCUSSION

This technique proved to be simple, sensitive, linear, and accurate for the simultaneous determination of NAP and DOM in combined dosage forms. In the initial phase of the study, absorption spectra of NAP (5-100 µg/mL) and DOM (1-100 µg/mL) (fig.4) were recorded using quartz cuvettes with a 1 cm path length, employing 0.1N NaOH as the reference solution in the UV region. The recorded spectra exhibited considerable variability, lacking well-defined absorption peaks and showing significant spectral overlap, particularly within the 200–400 nm range. This interference hindered the direct quantification of individual components. To overcome this challenge, the spectra were converted into their first-order derivatives, which improved the considerable variability between the two compounds. The zero-crossing method was then applied to identify wavelengths at which one drug displayed zero absorbance while the other produced a measurable signal. Specifically, 255 nm was identified as the zero-crossing point of NAP, enabling the determination of DOM, while 283.5 nm was the zero-crossing point of DOM for the analysis of NAP. These wavelengths were carefully selected to provide adequate spectral separation between the two drugs.

The method was validated through key analytical parameters, including linearity, accuracy, limit of detection (LOD), and limit of quantitation (LOQ). The method demonstrated excellent linearity within the concentration ranges of 5–100 µg/mL for NAP and 1–100 µg/mL for DOM, with correlation coefficients of 0.999 and 0.998, respectively. Recovery studies showed consistent performance, with recoveries ranging from 97.91% to 102.39% for NAP and from 99.33% to 101.25% for DOM. The LOD and LOQ were found to be 1.09 and 3.30 for NAP and 1.096 and 3.32 for DOM respectively. Precision studies showed low %RSD values, with intra-day values of 0.28% for NAP and 0.7% for DOM, and inter-day values of 0.35% for NAP and 1.3% for DOM, confirming the method's reliability and reproducibility.

In addition to analytical performance, the method's environmental sustainability was assessed using four green chemistry tools: Analytical Eco-Scale, GAPI, BAGI, and AGREE. The method received an Eco-Scale score of 80, indicating it is green, while AGREE yielded a moderate score of 0.48. GAPI and BAGI evaluations also reflected a moderately green profile, with scores of 68 and 67.5, respectively These results highlight the method's balance between analytical efficiency and environmental responsibility, with potential for further improvement by reducing solvent toxicity and waste generation.

GREENNESS EVALUATION OF THE PROPOSED METHODS

To evaluate the environmental sustainability of the developed first-order derivative spectrophotometric method for the simultaneous estimation of Naproxen (NAP) and Domperidone (DOM), various established green chemistry evaluation tools were used, including the Analytical Eco-Scale, GAPI (Green Analytical Procedure Index), BAGI (Blue Analytical Greenness Index), and AGREE (Analytical GREEnness Metric). The Analytical Eco-Scale evaluates the overall greenness of an analytical method by starting from a score of 100 and subtracting penalty points for factors such as the use of hazardous chemicals, energy requirements, and waste generation. [24][25] In this study, the method scored 80, indicating it is considered green, with penalties primarily due to the use of methanol and sodium hydroxide, which are known for their toxicity and corrosiveness. The GAPI tool provides a visual color-coded representation of the environmental impact across the entire analytical procedure, from sample collection to detection.[20][21] The method showed a mix of green, yellow, and red zones, with an overall score of 68, suggesting a moderately green profile but highlighting areas that could be improved, such as solvent use and waste handling. Similarly, the BAGI tool evaluates both practical usability and environmental safety through a blue-shaded diagram [22][23]. The method scored 67.5, indicating a satisfactory level of greenness, although further enhancements in solvent selection and waste reduction would be beneficial. Lastly, the AGREE tool integrates all twelve principles of green analytical chemistry into a single circular diagram with a final score ranging from 0 to 1.[26][27] The method achieved a score of 0.48, reflecting moderate greenness, with lower scores observed for areas involving hazardous solvents, energy usage, and lack of waste treatment. Overall, the greenness evaluation suggests that the method is environmentally acceptable, though there is possibility for making it safer and more

sustainable by reducing toxic reagents and minimizing waste.

Fig 8: GREENness eveluation as per GAPI, BAGI and AGREE

CONCLUSION

The developed UV spectrophotometric method employing first-order derivative spectrometry and the zero-crossing technique proved to be a simple, sensitive, accurate, and reliable approach for the simultaneous determination of Naproxen (NAP) and Domperidone (DOM) in combined dosage forms. By effectively addressing the spectral overlap in the 200–400 nm range, the use of derivative spectrophotometry enabled clear distinction and quantification of both drugs at their respective zero-crossing wavelengths (255 nm for DOM and 283.5 nm for NAP). The method showed excellent linearity, high recovery rates, low detection and quantitation limits, and minimal variability in precision studies.

The proposed derivative spectrophotometric method is moderately green, as confirmed by Eco-Scale, GAPI, BAGI, and AGREE evaluations. While it demonstrates good analytical performance, improvements such as using safer solvents and better waste management could enhance its environmental sustainability.

ACKNOWLEDGEMENTS

The authors express their sincere thanks to Himalayan Pharmacy Institute, Majhitar, India, for providing the necessary facilities to carry out this work. The authors are also grateful to MacLeods Pharmaceuticals Ltd., Sikkim, for kindly providing pure samples of Naproxen and Domperidone, which greatly helped in completing this study.

REFERENCES

1. Gharib A, Daneshtalab M, F. Bamoharram F, Roshani M, Jahangir M. One-pot synthesis of (S)-2-(6-methoxynaphtalen-2-yl)propanoic acid, (S)-Naproxen using Preyssler and Keggin-type heteropolyacids as green and reusable catalysts. Polish Journal of Chemical Technology - POL J CHEM TECHNOL. 2009 Oct 9;11:8–14. doi:10.2478/v10026-009-0029-7
2. Tehrani E, Faraji AR, Shojaei N, Shahinmehr S, Najafi A, Hekmatian Z, et al. An overview of the characteristics, toxicity, and treatment methods for the degradation of pharmaceutically active compounds: Naproxen as a case study. Journal of Environmental Chemical Engineering. 2023 Dec 1;11(6):111575. doi:10.1016/j.jece.2023.111575
3. Mostafa NS, Ayish NS, Abdel Rahman MA. A simple eco-friendly spectrofluorimetric resolution approach for the simultaneous determination of Naproxen and Domperidone in pharmaceutical formulation and human plasma; assessment of method greenness. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2025 Feb 5;326:125168. doi:10.1016/j.saa.2024.125168
4. Rekha Rout S, Kenguva G, Giri L, Dandela R. Novel salts of the antiemetic drug domperidone: synthesis, characterization and physicochemical property investigation. CrystEngComm. 2023;25(4):513–24. doi:10.1039/D2CE00902A
5. Tehrani E, Faraji AR, Shojaei N, Shahinmehr S, Najafi A, Hekmatian Z, et al. An overview of the characteristics, toxicity, and treatment methods for the degradation of pharmaceutically active compounds: Naproxen as a case study. Journal of Environmental Chemical Engineering. 2023 Dec 1;11(6):111575. doi:10.1016/j.jece.2023.111575
6. Reddymasu SC, Soykan I, McCallum RW. Domperidone: review of pharmacology and clinical applications in gastroenterology. Am J Gastroenterol. 2007 Sep;102(9):2036–45.doi:10.1111/j.1572-0241.2007. 01255.x PubMed PMID: 17488253.
7. Simultaneous determination of domperidone and Itopride in pharmaceuticals and human plasma using RP-HPLC/UV detection: Method development, validation and application of the method in in-vivo evaluation of fast dispersible tablets - PubMed [Internet]. [cited 2026 May 8]. Available from: https://pubmed.ncbi.nlm.nih.gov/26773534/
8. Barone JA. Domperidone: a peripherally acting dopamine2-receptor antagonist. Ann Pharmacother. 1999 Apr;33(4):429–40. doi:10.1345/aph.18003 PubMed PMID: 10332535.
9. Mondal MS, Haque MA, Islam MS, Islam SMA. Development and Validation of RP-HPLC Method for the Simultaneous Estimation of Domperidone and Naproxen in Tablet Dosage Form. J App Pharm Sci. 2011 Sep 30;:(Issue):145–8.
10. Guirguis KM, Zeid MM, Shaalan RA, Belal TS. HPLC-Fluorescence Detection Method for Concurrent Estimation of Domperidone and Naproxen. Validation and Eco-Friendliness Appraisal Studies. J Fluoresc. 2023 May;33(3):945–54. doi:10.1007/s10895-022-

03067-1 PubMed PMID: 36538143; PubMed Central PMCID: PMC10140086.

11. Singh S, Sharma S, Yadav A, Gautam H. SIMULTANEOUS ESTIMATION OF NAPROXEN AND DOMPERIDONE USING UV SPECTROPHOTOMETRY IN TABLET DOSAGE FORM. In. 2013 [cited 2026 May 12]. Available from: https://www.semanticscholar.org/paper/SIMULTANEOUS-ESTIMATION-OF-NAPROXEN-AND-DOMPERIDONE-Singh-Sharma/eda0babaf7060fe64c0205c24668091d3dcf5361
12. Prabu SL, Shirwaikar A, Shirwaikar A, Kumar CD, Joseph A, Kumar R. Simultaneous Estimation of Esomeprazole and Domperidone by UV Spectrophotometric Method. Indian J Pharm Sci. 2008 Jan;70(1):128–31. doi:10.4103/0250-474X.40351 PubMed PMID: 20390100; PubMed Central PMCID: PMC2852053.
13. Kaushik KN, Banerjee SK. UV Spectrophotometric Method Development for the Determination of Domperidone in Tablet Formulation. Asian Journal of Research in Chemistry. 2009 Dec 28;2(4):432–3.
14. Lotfy H, Sm A, He Z, Ns M. Spectrophotometric Methods for Quantitative Determination of Binary Mixture of Naproxen Sodium and Domperidone Maleate 2768.
15. Patel B, Patel M, Patel J, Suhagia B. Simultaneous Determination of Omeprazole and Domperidone in Capsules by RP-HPLC and Densitometric HPTLC. Journal of Liquid Chromatography & Related Technologies. 2007 May 1;30(12):1749–62. doi:10.1080/10826070701360368
16. R TR, H KM, S SG, J BR. A Review on Simultaneous Estimation of combination of Omeprazole and Domperidone in Bulk and Tablet by RP-HPLC Method. Research Journal of Pharmacy and Technology. 2024 May 15;17(5):2409–12. doi:10.52711/0974-360X.2024.00377
17. Gondalia R, Dharamsi A. Simultaneous estimation of Samaritan succinate and naproxen sodium in bulk drug and pharmaceutical dosage form by RP-HPLC method. Journal of Drug Delivery and Therapeutics. 2013 Mar 15;3(2). doi:10.22270/jddt.v3i2.463
18. Pasquini C. Near infrared spectroscopy: A mature analytical technique with new perspectives – A review. Analytica Chimica Acta. 2018 Oct 5;1026:8–36. doi:10.1016/j.aca.2018.04.004
19. Płotka-Wasylka J. A new tool for the evaluation of the analytical procedure: Green Analytical Procedure Index. Talanta. 2018 May 1;181:204–9. doi:10.1016/j.talanta.2018.01.013
20. Gałuszka A, Migaszewski Z, Namieśnik J. The 12 principles of green analytical chemistry and the SIGNIFICANCE mnemonic of green analytical practices. TrAC Trends in Analytical Chemistry. 2013 Oct 1;50:78–84. doi:10.1016/j.trac.2013.04.010
21. Manousi N, Wojnowski W, Płotka-Wasylka J, Samanidou V. Blue applicability grade index (BAGI) and software: a new tool for the evaluation of method practicality. Green Chem. 2023;25(19):7598–604. doi:10.1039/D3GC02347H
22. Aken KV, Strekowski L, Patiny L. EcoScale, a semi-quantitative tool to select an organic preparation based on economical and ecological parameters. Beilstein J Org Chem. 2006 Mar 3;2(1):3. doi:10.1186/1860-5397-2-3
23. Mohr A, Camboim B, Mendez A, Garcia C, Steppe M. Overview of the Greenness' Metrics used to Evaluate Analytical Methods. Braz J Anal Chem. 2025 Jun 4. doi:10.30744/brjac.2179-3425.RV-1-2025
24. Pena-Pereira F, Wojnowski W, Tobiszewski M. AGREE-Analytical GREEnness Metric Approach and Software. Anal Chem. 2020 Jul 21;92(14):10076–82. doi:10.1021/acs.analchem.0c01887 PubMed PMID: 32538619; PubMed Central PMCID: PMC7588019.
25. Tobiszewski M. Metrics for green analytical chemistry. Anal Methods. 2016 Apr 15;8(15):2993–9. doi:10.1039/C6AY00478D