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Original Article

Assessment and Comparison of Greenness of UV-Spectroscopy Methods for Simultaneous Determination of Anti-Hypertensive Combination

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ABSTRACT

Background: Environmentally destructive analytical research practices, such as using and releasing hazardous solvents and reagents into the atmosphere, have brought up serious concerns regarding the ecological impact of these actions. By checking greenness of the methods, ecological challenges can be minimized. This gives a brief idea about its extent of effect on environment to the analyst. **Aim:** This work was designed to select the ecofriendly method for the estimation of amlodipine besylate and telmisartan from the existing UV spectroscopy methods. **Materials and Methods:** In this work the methods available to estimate these two drugs by UV-spectroscopy are collected and assessed in terms of their greenness using a variety of green metrics like National Environmental Method Index, Raynie and Driver tool/AGP, Analytical Eco Scale and AGREE. This considers the Green Analytical Chemistry twelve principles. **Results and Conclusion:** The degrees of greenness for the selected methods were shown as pictograms for some metrics and scores in some other cases using the assessment tools. The greenness of the selected methods was tabulated and compared for the best choice. The study gave a clear idea about the pros and cons of the methods with respect to greenness and made it easy for the analyst to select the best eco-friendly method.

Keywords: Green analytical chemistry, Green Metrics, UV-spectroscopy, Eco-friendly, Green solvents.

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INTRODUCTION

Hypertension is the primary controllable risk factor and a heart disease is the primary cause of death in the world. When Blood Pressure (BP) is less than 115/75 mmHg, this is the lowest risk point for cardiovascular disease. Beyond this point, every 10 mm Hg increase in either the Systolic (SBP) or Diastolic (DBP) Blood pressure raises the chance of significant heart and stroke incidents by two. Lowering the blood pressure has several advantages, one of which is the decreased risk of cardiovascular death. It takes two or more anti-hypertensive medications to treat hypertension in more than two thirds of individuals in order to reach target blood pressure.[1] Amlodipine and telmisartan lowers blood pressure through complimentary processes that work in concert to lower blood pressure.[2]

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Angiotensin II receptors blockers or ARBs are well-tolerated and efficient anti-hypertensive medications that work by obstructing the renin-angiotensin-aldosterone pathway, which in turn prevents aldosterone production, vasoconstriction and salt retention. Due to its elimination half-life of around 24 hr, telmisartan, an ARB with significant AT1 receptor selectivity has been shown to lower Blood Pressure (BP) for a full day when taken once daily. Another popular long-acting antihypertensive medication is amlodipine besylate, a Calcium Channel Blocker (CCB).[3]

Amlodipine besylate is also known as benzenesulfonic acid:3-*O*-ethyl 5-*O*-methyl 2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-6-methyl-1,4-dihydropyridine-3,5-dicarboxylate.

Figure 1 shows the chemical structure of Amlodipine besylate. It is a part of a medication category known as dihydropyridine calcium channel blockers, which is used in conjunction with other drugs or alone to treat angina and excessive blood pressure. It is a frequently prescribed cardiovascular medication and an antagonist of third generation which are characterized by maintaining tissue selectivity and demonstrating favorable pharmacokinetic profile.[4]

Chemically telmisartan is 2-[4-[[4-methyl-6-(1-methylbenzi midazol-2-y1)-2-propylbenzimidzol-1-yl] methyl] phenyl1] benzoic acid. Telmisartan lowers blood pressure by attaching itself to the Type 1 angiotensin II receptor and preventing vascular smooth muscle cells from being affected by angiotensin II. Recent research has demonstrated that telmisartan possesses PPAR-gamma agonistic characteristics as well, which may have positive metabolic effects. When the 40 mg dose is taken with food, there is a 6% reduction in effectiveness.[5] Targeting the Angiotensin 1 (AT1) receptor subtype, telmisartan is a strong nonpeptide angiotensin II antagonist which has a long half-life. 40-80 mg once daily is an effective dose of telmisartan.[6] Figure 2 displays the structure of Telmisartan.

Amlodipine besylate and telmisartan in combination produces a considerable 24 hr blood pressure efficacy that is superior to either medication alone or in individuals with stage 1 or 2 hypertension.[7] This study aims to address several contemporary and fundamental analytical techniques that have been created for the purpose of estimating medications such as Telmisartan and amlodipine besylate and to assess them for greenness with keeping factor such as environmental impact to check how well it can align with green chemistry principles.

Developing analytical methods for figuring out pharmaceutical dosage forms or bulk drugs is challenging due to the complexity and variety of substances. Many analytical specialists from various disciplines have worked very hard to create a distinct, trustworthy analytical technique that conforms to legal and regulatory requirements. Regulators are searching for more ecological methods for minimizing or getting rid of the creation of hazardous Analytes, solvents and chemical contamination of effluents in analytical departments.[8]

Green Analytical Chemistry (GAC)

Many criteria have been put out for evaluating greenness since the notion of Green Analytical Chemistry (GAC) which was first brought into existence on the year of 2000.[9] Chemicals and techniques are used by all industries, including engineering, pharmaceutical and chemicals to test their products. Recently, in order to prevent pollution, scientists have been focusing on creating environmentally friendly analytical techniques by using green chemistry. To ensure environmental friendliness, the developed technique must adhere to the principles of GAC.[10]

Recognizing GAC's contribution to the advancement of Analytical chemistry is very crucial. The main challenge in this profession is to strike a balance between increasing the environmental friendliness of analytical techniques and producing higher-quality results. The implementation of the principles that form the basis of GAC is necessary to address this challenge.

Anastas and Warner created 12 GAC principles in 1998 by keeping synthetic chemistry in mind. This method of application involves the following ideas for both synthesis and analysis.

i) Waste prevention,

ii) Safer auxiliaries and solvents,

iii) Energy-efficient design,

iv) Derivatization reduction.

Furthermore, an effort was undertaken to ascertain the analytical consequences of the 12 green chemistry principles. Regrettably, a minimum of one principle which is, optimization of atom economy, also known as principle number two is inadequate for analytical chemistry. Moreover, the 12-point framework proposed by Anastas and Warner omits a few key concepts included in GAC. According to studies, these 12 green chemistry principles need to be modified for analytical chemistry to fully benefit from them.[11]

The following Figure 3 represents the 12 principles of GAC.

The main tenet of "green chemistry" is to reduce hazards in the nature and to promote public health thereby decreasing production, design and use of such chemicals through proper knowledge, therefore it is now more important to prevent or reduce the production of toxic waste than it is to treat the waste that has already been produced.

Green metrics

The National Environmental Method Index (NEMI), Analytical Eco-scale, GAPI (Green Analytical Procedure Index) and AGREE (Analytical Greenness) are the most comprehensive metrics for evaluating hazard effects of analytical techniques on environment, other metrics, like the HPLC-EAT and AMVI, have been specifically developed to use for HPLC determinations.

AGREE, GAPI, NEMI and Eco-scale were the most often utilized methods.[12] Analytical chemistry relies on measurements qualitatively and quantitatively with the help of green metrics, in this field more knowledge can be gained[13] As discussed above these Green analytical metrics work on the 12 principles of GAC which includes technique such as utilization of tiny sample proportions, low energy and chemical usage, the use of recyclable and renewable resources and minimal waste production.

MATERIALS AND METHODS

Approaches for the simultaneous estimation of telmisartan and amlodipine besylate using UV spectrometry that have been published thus far are discussed below.

M.S. Kondawar, K.G. Kamble *et al.*, (2011) developed a straightforward, precise and repeatable spectrophotometric technique for the measurement of Amlodipine besylate (AML) and Telmisartan (TEL) simultaneously in combined tablet dosage forms. The multi wavelength approach is adopted in the wavelength of 298 nm and 360 nm with the concentration ranges of 1-10 mcg/mL^{-1} and 15-75 mcg/mL respectively, with average recovery of 98% for both drugs. A High degree of precision is shown by the methods with low computed standard deviation and RSD. Additionally, RSD lower than 2% as mandated by ICH rules and also showed recovery percentage ranged from 98-102%, demonstrating good specificity and accuracy of the suggested approach.[14]

K. P. Hirpara *et al.*, (2012) proposed two spectrophotometric techniques for determining Telmisartan and Amlodipine besylate in tablet formulation simultaneously. The first approach is called the absorbance correction method, which is based on figuring out the absorptivity value of amlodipine besylate at 362 nm and the concentration of Telmisartan at 292 nm. Significant absorption is not observed in TELM. As a result, these wavelengths were used to estimate TELM and AMLB. Both wavelengths' absorbances were measured. The second method, called absorbance ratio, used 292 nm as Telmisartan's λ_{max} and 326 nm as an isoabsorptive point. Upon overlaying the spectra of AMLB and TELM, it was observed that the isoabsorptive point for AMLB estimation was at 326 nm, whereas the λ_{max} for TELM estimation was at 292 nm. After calculating the absorbance and absorptivity, these values were entered into equations 1 and 2 to determine the drug concentration. For AMLB and TELM, linearity is observed in the concentration range of 0.5-2.0, 0.5-15.5 mcg/mL and 3-24 mcg/mL, respectively, using methods A and B.[15]

Shinde Prasad S. Patil Pallavi M *et al.* (2014) developed a method for the purpose of determining the combined dosage form of amlodipine besylate and telmisartan, where two straightforward, quick, accurate and exact spectrophotometric procedures have been devised, utilizing the simultaneous equation method and stability study method. The two wavelengths such as 242 nm and 231 nm are selected for quantification of AML and TML which is a foundation for simultaneous approach. The concentration range of 2-7 μg/mL for Telmisartan and 5-30 μg/mL for Amlodipine where both techniques complied with Beer's law. The ICH proposed differing settings for the stress degradation of amlodipine and Telmisartan. The devised method was applied to the samples produced in this way to study degradation. The author suggested that techniques were approved and can be applied to the examination of a combination dosage tablet formulation that includes Telmisartan and Amlodipine and this work serves as an illustration of how to create a stability indicating test method for TEL and AMB in which forced degradation was done under all stress scenarios. These medications show deterioration in every condition examined. But there was a difference in the degree of deterioration. The technique created for the quantitative measurement of TEL and AMB is quick, accurate, selective and exact. These techniques can be effectively used for regular quality control examinations of AMB and TEL because the validation test results were determined to be satisfactory.[16]

R. L. C. Sasidhar *et al.,* (2014) created a precise, affordable and repeatable UV-spectrophotometric technique for the simultaneous measurement of telmisartan, amlodipine besylate and hydrochlorothiazide in tablet and also bulk dose forms. The necessary dilutions with distilled water were made after the stock solutions were produced in methanol. Using this method, simultaneous equations for the absorbance maxima of hydrochlorothiazide, amlodipine besylate and telmisartan are formed and solved at 272, 360 and 296 nm, respectively. Beer's law was followed in the following concentration range of 2-12 mcg/mL, 10-70 mcg/mL and 2-20 mcg/mL for telmisartan, hydrochlorothiazide and amlodipine besylate, respectively. Recovery studies and statistical validation were conducted on the analysis results. For the recovery study, the percentage RSD was less than 2. The suggested approach can be used successfully to estimate these three medications simultaneously in combination tablet dosage form and in bulk.[17]

Gupta NK *et al.*, (2015) has described easy, reliable and repeatable spectrophotometric techniques for estimating Amlodipine besylate (AML) and Telmisartan (TEL) Simultaneously in combination tablet dose forms. The sample wavelengths chosen for the method are TLM=297 nm and AML=238 nm, covering concentration ranges of 8-48 μg/mL for TEL and 1-6 μg/mL for AML, respectively. The approach requires the use of the simultaneous equation method for determination. The procedure was verified in compliance with ICH recommendations for applicability for assay, linearity, accuracy, precision and robustness. The regular quality control for the simultaneous analysis of Amlodipine besylate (AML) and Telmisartan (TEL) could benefit from the use of the suggested method, which is easy to use, affordable, accurate and exact.[18]

Deepali M. Gangrade and Priyanka Y. Kulkarni (2016) produced a novel approach to simultaneously determine Amlodipine besylate, telmisartan and hydrochlorothiazide in combination tablet dosage form using a UV-spectrophotometric absorption correction method that is easy to use, sensitive and accurate. For amlodipine besylate, telmisartan and hydrochlorothiazide, the chosen wavelengths for the analysis were 365 nm, 250 nm and 335 nm, respectively. Beer's law was followed from the concentration ranges of 10-60 μgmL^{-1}, 4-20 μg/mL and 20-100 μgmL^{-1} for hydrochlorothiazide, telmisartan and amlodipine besylate, respectively. The solvents that were utilized were methanol and distilled water. The range of the percentage recovery was determined to be 99.8% to 101.2% for HCT, 99.6% to 101.3% for TEL and 98.9% to 101.6% for AMB. A statistical validation was performed on the developed approach. Less than two was discovered to be the% RSD value. As a result, the suggested method was easy to use, economical, quick, accurate and exact. It can also be effectively used to determine amlodipine besylate, telmisartan and hydrochlorothiazide simultaneously in the form of mixed tablet dosage.[19]

G. K. Dyade *et al.*, (2022) created Quality by Design, which is used in the creation of analytical techniques as well as other pharmaceutical procedures. A chemometric-based analytical method was created using the QbD approach to estimate telmisartan and amlodipine besylate using UV-visible spectrophotometry. The absorbance was measured at wavelengths of 291.2 nm and 365.2 nm using a solvent of 0.1 N HCl. In order to choose the important parameters, the impact of input factors on spectrum features was examined. The created approach was then validated in accordance with ICH Q2 R1 regulatory criteria. The concentration range of 5-40 mcg/mL was used to determine the linearity of both medications. The precision investigation revealed acceptable data as %RSD 2.5416 for telmisartan and 5.7364 for AML. The accuracy was found to be 104.46% for TEL and 96.25% for AMD. For the estimation of AMD and TEL, which are in 1: 8 proportional in dosage form composition, the developed approach is inflexible, reliable and effective. By defining the design area later on and doing risk assessment early on, QbD was used to develop a strict, reliable approach.[20]

Methods and their Parameter adopted while estimating the Amlodipine besylate and Telmisartan so far are discussed in Table 1.

Utilization of the green analytical tools to above methods

NEMI: (National Environmental Method Index)

The NEMI profile criteria are depicted using a pictogram that has four fields indicating the use of hazardous, poisonous, or corrosive reagents, as well as the generation of substantial amounts of waste during the procedure. If the chemicals utilized are not persistent, dangerous and non-corrosive (pH range 2 to 12), with the quantity of waste produced is less than 50g, then the corresponding quadrant of the NEMI pictograms will show green color. If the approach does not meet that specific condition, the NEMI pictogram's quadrants remain blank (5). Although the NEMI pictogram approach is one of the fastest ways to calculate GAC metrics and yields qualitative findings, it is not comprehensive enough to convey the number of dangers.[21] NEMI parameters related to the methods used are discussed in Table 2.

Table 1: Depiction of methods and their parameters adopted to estimate Amlodipine besylate and Telmisartan.

Sl. No.	Methods	Reagents or solvents	Detection (nm) AML TML		Linearity (µg/mL) AML TML	
1	AML and TML estimation in bulk medication dose form using multi wavelength analysis.	Methanol	360	298	15-75	1-10
2.	Simultaneous estimation of Amlodipine besylate and Telmisartan in combination.	0.1 N HCl	362 and 326	292	Method A 0.5-20 Method B 0.5-15.5	Method A 3-24 Method B 3-24
3.	Determination of Amlodipine besylate in combination dose form using the simultaneous equation technique and stability study method.	0.1N NaOH	242	231	5-30	2-7
4.	Simultaneous measurement of combined tablet dose form and bulk amounts of Hydrochlorothiazide, Amlodipine besylate and telmisartan.	Methanol	365	250	10-60	4 -20
5	Simultaneous assessment of combined tablet dosage formulations containing Telmisartan and amlodipine besylate.	Methanol	238	297	1-6	8-48
6.	The simultaneous determination of Hydrochlorothiazide, telmisartan and amlodipine besylate in API and combination tablet dose formulation using and absorbance correction technique.	Methanol and water	365	250	10-60	4 - 20
7.	The utilization of QBD in the creation of chemometric assisted methods for telmisartan and amlodipine besylate.	0.1 N HCl	291.2	365.2	5-40	5-40

Raynie and Driver tool

A novel approach based on green chemistry properties was put out by Raynie *et al*. As a result, depending on the risk potential, it may be categorized into the following five categories such as waste, energy, safety, environmental and health. The NFPA classified the compounds with flammability score and level of toxicity in SECTION 704, based on that, the pentagram's color was filled in according to the rating.[22] The criteria considered while evaluating methods with respect to Raynie tool is listed in Table 3.

Analytical Eco-scale

Among the various green metrics in use, Analytical eco scale is a helpful tool for evaluating environmental friendliness of an analytical method. It considers and contrasts all of the analytical process's parameters and phases. Any element which does not obey flawless green analysis then it is penalized with points. Green analysis is considered best, if eco-scale rating is 100; if it is greater than 50, it is considered acceptable and if it's smaller than 50 then its insufficient environmental analysis. Each of the four primary areas where an analytical technique deviates from a best green analysis or ideal analysis is related to parameter such as quantity of reagent taken, hazardousness, energy consumption and waste production. Penalty points are allotted to the chemicals based on the distinct kinds of hazard such as physical, environmental, health and also Penalty points will vary according to reagent quantity.[23]

AGREE

The Green and Analytical Calculator (AGREE metric) was created by the Gdańsk University of Technology. The twelve parameters that determine the result of this software's calculation matches the twelve GAC principles. Each parameter or principle has a score ranging from 0 to 1, which is determined by the degree of risk associated with a certain principle's greenness. The principles of SIGNIFICANCE are used to compute the final score. The ultimate score with each criterion for analytical process performance and the user assigned weights are all displayed in a pictogram as the outcome. The AGREE tool symbolizes greenness as a traditional clock form with the numbers 1 to12 on the circle's periphery, signifying the 12-principles.[24] The greenness of taken methods are evaluated using AGREE tool and shown in Table 4.

RESULTS AND DISCUSSION

The GAC tools were applied to the reported methods as per the procedure mentioned above with respect 12 Principles of GAC. The pictogram obtained for each method depicts the method greenness with respect to its parameters. The detailed greenness assessment is shown in Table 5.

Table 2: NEMI Parameters compiled in relation to the employed techniques.

PBT Chemicals	Hazardous waste list	Corrosive	Waste
HCl (Listed in EPA's TRI list)	Methanol	Sodium hydroxide	Waste generated <50 g or mL=Green.
	HCl	HCl	Waste generated >50 g or mL=left blank.

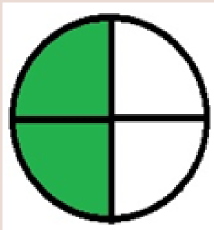
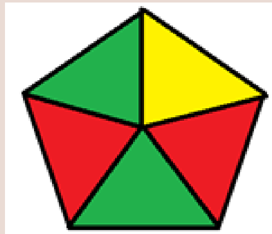
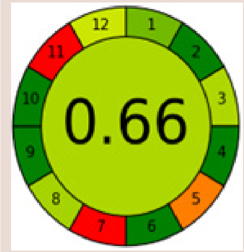
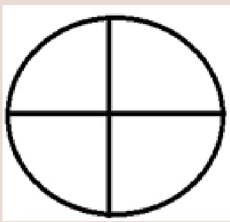
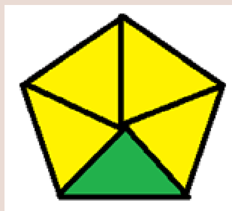
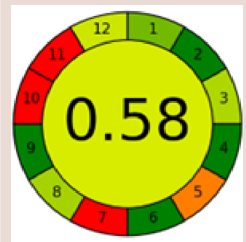
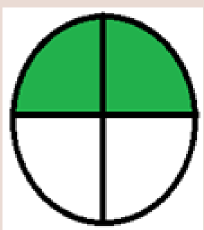
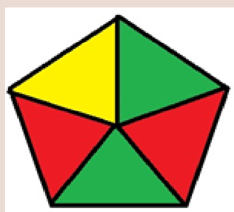
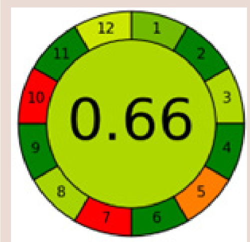
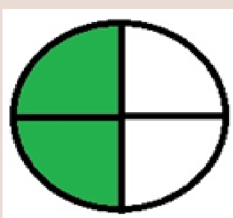
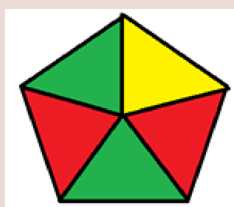
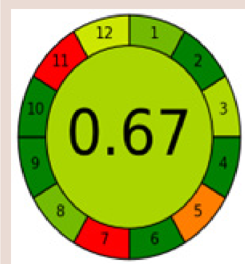
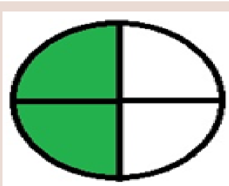
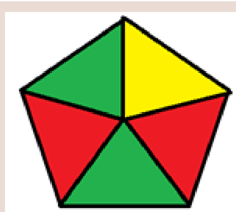
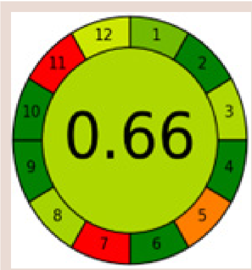
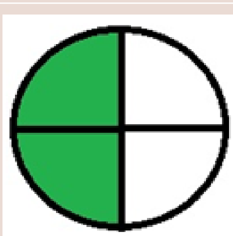
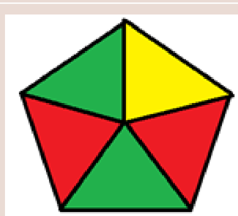
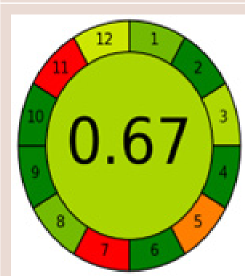
Table 3: Green evaluation criteria based on Raynie and Driver's tool.

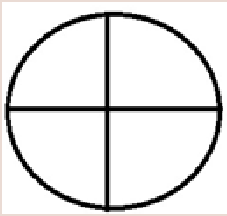
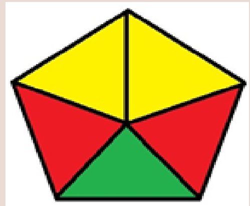
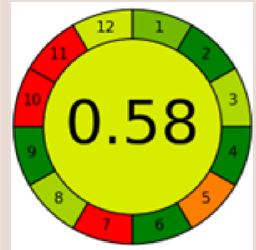
Sl. No.	Parameter	Green	Yellow	Red
1	Health hazard	NFPA listed slightly irritant chemicals. E.g.: Methyl alcohol, NaOH, Ethyl acetate.	Moderately noxious chemicals listed in NFPA list. E.g.: HCl, ACN, Formic acid.	Carcinogenic with NFPA score (4) E.g.: Hydro cyanide, Arsine.
2	Safety hazard	NFPA flammability score (0 or 1) with special hazard E.g.: NaOH	NFPA flammability score (2 or 3) E.g.: Methanol, Acetonitrile, Acetic acid.	NFPA flammability score (4) E.g.: Acetaldehyde, Acetylene.
3	Environmental hazard	Environmental hazard should be < 50 g	If Environmental hazard 50-250 g.	If Environmental hazard >250
4	Energy	Methods with less energy consumption E.g.: Titrations, UV-spectrometer.	Methods such as HPLC, UPLC and GC.	LC-MS, GC-MS
5	Waste amount	The total waste should be <50 g in sample analysis.	If the total waste is 51-250 g.	If the total waste is >250 g.

Table 4: The table illustrates the greenness of the aforementioned techniques which is assessed using the AGREE tool.

Sl. No.	Parameters	Method 1	Method 2	Method 3	Method 4	Method 5	Method 6	Method 7
1	Sampling procedure	Infield sampling and online analysis.	Infield sampling and online analysis.	Infield sampling and online analysis.	Infield sampling and online analysis.	Infield sampling and online analysis.	Infield sampling and online analysis.	Infield sampling and online analysis.
2	Amount of sample in g or mL.	45 mg	45 mg	45 mg	40 mg	45 mg	45 mg	45 mg
3	Positioning of the analytical device.	On-line	On-line	On-line	On-line	On-line	On-line	On-line
4	Number steps required in preparation of sample. Eg: extraction, Sonication, mineralization.	3 or fewer	3 or fewer	3 or fewer	3 or fewer	3 or fewer	3 or fewer	
5	Level of automation and preparation of sample.	Semi-automatic and Sample is not miniaturized.	Semi-automatic and Sample is not miniaturized.	Semi-automatic and Sample is not miniaturized.	Semi-automatic and Sample is not miniaturized.	Semi-automatic and Sample is not miniaturized.	Semi-automatic and Sample is not miniaturized.	Semi-automatic and Sample is not miniaturized.
6	Derivatization	None	None	None	None	None	None	None
7	Analytical waste	400 mL	220 mL	490 mL	615 mL	260 mL	960 mL	330 mL
8	Number of analytes determined.	2	2	2	3	2	3	2
9	The use of energy should be minimized.	UV-vis spectroscopy (<0.1 kWh/spl).	UV-vis spectroscopy (<0.1 kWh/spl).	UV-vis spectroscopy (<0.1 kWh/spl).	UV-vis spectroscopy (<0.1 kWh/spl).	UV-vis spectroscopy (<0.1 kWh/spl).	UV-vis spectroscopy (<0.1 kWh/spl).	UV-vis spectroscopy (<0.1 kWh/spl
10	Reagents	Biobased	Not biobased	Not biobased	Biobased	Biobased	Biobased	Not biobased
11	Toxic reagents	Methanol	0.1N HCl	No (0.1N NaOH)	Methanol	Methanol	Methanol	0.1N HCl
12	Operator safety	Hazardous to aquatic life and highly flammable.	Hazardous to aquatic life and corrosive.	Hazardous to aquatic life and corrosive.	Hazardous to aquatic life and highly flammable.	Hazardous to aquatic life and highly flammable.	Hazardous to aquatic life and highly flammable.	Hazardous to aquatic life and corrosive.

Table 5: The assessed results which are evaluated using GAC tools for aforementioned methods.

Methods	NEMI	Raynie and Driver tool	Analytical Eco-Scale	AGREE
Method 1			Amount PP×Hazard PP >100 mL reagent (3)×(2) PP for Methanol=6 Energy (<0.1 kWh/spl)=1 Waste (>10 mL)=5 No treatment=3 Analytical Eco-scale score 100-Total penalty points 100 - 15=85	
Method 2			>100 mL reagent (3)×(2) PP for HCl=6 Energy (<0.1 kWh/spl)=1 Waste (>10 mL)=5 No treatment=3 Analytical Eco-scale score 100-15=85	
Method 3			>100 mL reagent (3)×(2) PP for NaOH=6 Energy (<0.1 kWh/spl)=1 Waste (>10 mL)=5 No treatment=3 Analytical Eco-scale score 100-15= 85	
Method 4			>100 mL reagent (3)×(2) PP for Methanol= 6 Energy (<0.1 kWh/spl)=1 Waste (>10 mL)=5 No treatment=3 Analytical eco-scale score 100-Total penalty points 100-15=85	
Method 5			>100 mL reagent (3)×(2) PP for Methanol=6 Energy (<0.1 kWh/spl)=1 Waste (>10 mL)=5 No treatment=3 Analytical Eco-scale score 100-15=85	
Method 6			>100 mL reagent (3)×(2) PP for Methanol= 6 Energy (<0.1 kWh/spl)=1 Waste (>10 mL)= 5 No treatment=3 Analytical Eco-scale score 100-Total penalty points 100-15=85	

Methods	NEMI	Raynie and Driver tool	Analytical Eco-Scale	AGREE
Method 7			>100 mL reagent (3)×(2) PP for HCl=6 Energy (<0.1kWh/spl)=1 Waste (>10 mL)=5 No treatment=3 Analytical Eco-scale score 100-15=85	

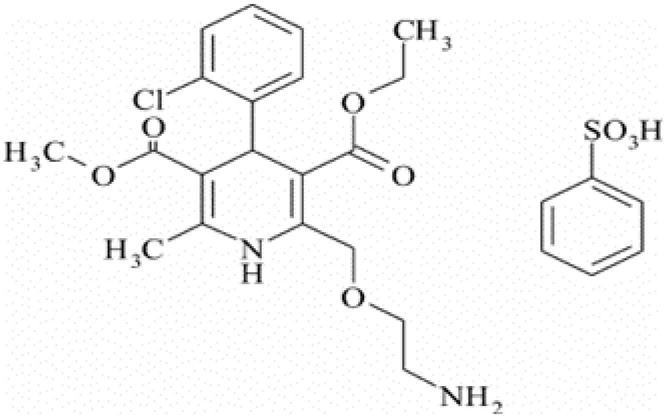


Figure 1: The Amlodipine Besylate structure.

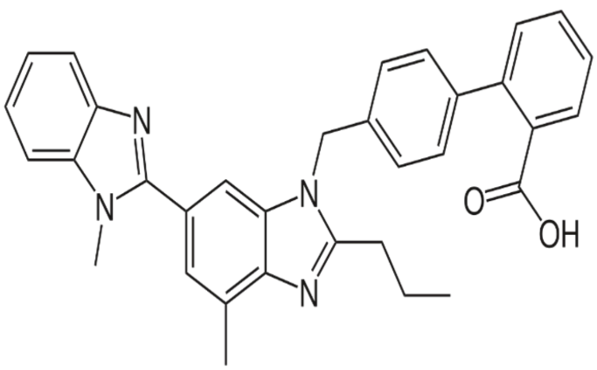


Figure 2: Structure of Telmisartan.

Figure 3: The GAC's twelve Guiding Principles.

According to the above evaluation with respect to GAC tools, all methods are evaluated keeping environmental aspects in main focus, therefore. In case of NEMI tool except method 2 and 7, all the pictograms are showing green color in two quadrants which explains that other methods are comparatively greener. The Raynie and Driver tool indicates that method two is relatively greener with respect to its five parameters such as, safety hazard, health hazard, Environmental hazard, waste and Energy generated. In Analytical Eco scale, all of the procedures had scores of 85, meaning they are all green in terms of the penalty points assigned for the evaluation approaches used. For AGREE, Method 4 and Method 6 is comparatively greener with a score of 0.67, indicating relative greenness compared to other methods, whereas method2 and method 7 with a score of 0.58 showed less greenness and also other reported methods are moderately green in comparison.

CONCLUSION

The Ecofriendly nature of all the reported analytical methods for Simultaneous estimation of Amlodipine besylate and telmisartan by UV-spectroscopy was evaluated using green metrics, which were developed by considering GAC principles. By considering the above attributes into account, Method 4 and method 6 was found to be comparatively greener by obeying some GAC principles whereas method 7 shows less greenness aspects in terms of evaluation result and the remaining methods were moderately green. Hence there is a need to develop a novel method which is still more ecofriendly as well as obeys all principles of GAC. In addition to this recently evolved White Analytical Chemistry (WAC) principles can also be considered in developing a new UV analytical method that supports sustainability.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

GAC: Green Analytical chemistry; **NEMI:** National Environmental Method Index; **AGREE:** Analytical GREEnness; **AGP:** Analytical Greenness Profile; **PBT:** Persistent Bio accumulative Toxic; **TRI:** Toxic Release Inventory; **PP:** Penalty Points; **NFPA:** National Fire Protection Association.

SUMMARY

Eco-friendly nature of the existed UV spectroscopic methods for the simultaneous estimation of amlodipine besylate and telmisartan were assessed using green metrics. The green metrics utilized for the study were NEMI, AGP, AES and AGREE. The obtained results were assessed and compared. The study revealed method 4 and 6 are more greener than the other existed methods.

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