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GREEN ANALYTICAL TRENDS IN UV SPECTROPHOTOMETRIC METHODS FOR PREGABALIN AND ETORICOXIB: A COMPARATIVE REVIEW AND GREENNESS ASSESSMENT

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ABSTRACT

The principles of Green Analytical Chemistry (GAC) emphasize reducing hazardous chemicals, minimizing waste, and adopting energy-efficient methods in pharmaceutical quality control. UV spectrophotometry, due to its simplicity, cost-effectiveness, and lower environmental burden, is considered a greener alternative to chromatographic techniques. This review critically evaluates UV spectrophotometric methods for Pregabalin (PGB) and Etoricoxib (ETX) using two greenness metrics: the Analytical GREEnness Metric (AGREE) and the Green Analytical Procedure Index (GAPI).

Eight Pregabalin methods (Refs 1–8) and seven Etoricoxib methods (Refs 9–15) were assessed. Pregabalin methods required derivatization with reagents such as DNPH, MBTH, vanillin, and ninhydrin, typically in hazardous solvents like methanol and DMF. These methods yielded AGREE scores between 0.61 and 0.74, with GAPI pictograms showing red zones in derivatization and solvent use but green in instrumentation. In contrast, Etoricoxib methods relied mostly on direct UV analysis in aqueous or mildly acidic/alkaline media, producing AGREE scores between 0.65 and 0.71, with GAPI profiles dominated by green and yellow fields and only occasional red zones from organic solvent use.

Overall, Etoricoxib methods demonstrated more consistent greenness, while Pregabalin methods showed greater variability due to derivatization requirements. This comparative review highlights the importance of solvent selection, derivatization-free approaches, and greenness evaluation in pharmaceutical analysis.

Keywords: Green Analytical Chemistry (GAC), pharmaceutical quality control. UV spectrophotometry, Pregabalin (PGB) and Etoricoxib (ETX)

1. INTRODUCTION

The application of analytical chemistry in the pharmaceutical industry is indispensable for ensuring drug quality, safety, and efficacy. However, conventional analytical methods often consume large volumes of toxic solvents, require energy-intensive instrumentation, and generate considerable chemical waste. Such practices conflict with the principles of environmental sustainability.

The emergence of Green Analytical Chemistry (GAC) in 2000 marked a significant step toward reducing the ecological impact of analytical sciences. By adapting the 12 principles of green chemistry originally introduced by Anastas and Warner (1998), GAC promotes environmentally benign analytical methods through direct analysis, waste minimization, safer solvents, and energy efficiency. The challenge lies in balancing sustainability with analytical performance, ensuring that greener methods remain reliable, sensitive, and reproducible.

Among available analytical techniques, UV spectrophotometry stands out as a relatively greener tool compared to separation-based methods such as HPLC. Its advantages include minimal sample preparation, low reagent consumption, reduced waste generation, and lower energy demands. Nevertheless, the greenness of UV procedures depends on method-specific factors such as derivatization, solvent selection, and waste management.

Pregabalin

Pregabalin (PGB) is a structural analogue of the inhibitory neurotransmitter γ-aminobutyric acid (GABA) and is widely used in the treatment of neuropathic pain, epilepsy, generalized anxiety disorder, and fibromyalgia **[16]**. Its mechanism of action involves binding to the α2-δ subunit of voltage-gated calcium channels in the central nervous system, thereby reducing the release of excitatory neurotransmitters such as glutamate and substance P.

Chemically, Pregabalin is *(S)-3-(aminomethyl)-5-methylhexanoic acid*, a small aliphatic molecule with no extended

conjugated system, and thus lacks strong intrinsic chromophores for UV detection. This structural feature explains its absence of intrinsic UV chromophores and the analytical necessity for derivatization **(Figure 1)**. To overcome this, spectrophotometric assays typically involve derivatization with chromogenic reagents such as DNPH, MBTH, Gibb's reagent, vanillin, benzoyl chloride, or ninhydrin **[1–8]**. While effective, these derivatization steps increase chemical consumption, introduce toxic solvents such as methanol or DMF, and generate additional waste — all of which reduce the overall greenness of the methods. Consequently, Pregabalin is a challenging candidate for green UV spectrophotometry.

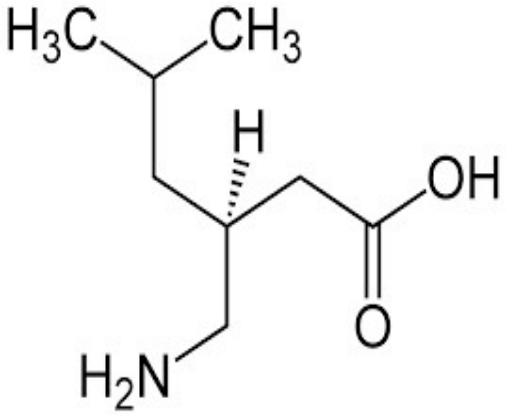


Figure 1: Chemical structure of Pregabalin

Etoricoxib

Etoricoxib (ETX) is a highly selective cyclooxygenase-2 (COX-2) inhibitor belonging to the coxib class of non-steroidal anti-inflammatory drugs (NSAIDs). Clinically, it is indicated for the management of osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, gout, and acute pain **[17]**. Compared to traditional NSAIDs, Etoricoxib provides anti-inflammatory and analgesic benefits with a reduced incidence of gastrointestinal side effects due to its COX-2 selectivity.

Structurally, Etoricoxib is *5-chloro-6'-methyl-3-[4-(methylsulfonyl)phenyl]-2,3'-bipyridine*. The presence of aromatic and heteroaromatic rings with extended conjugation confers strong intrinsic UV absorbance in the range of 233–301 nm **[9–15]**. These chromophoric groups allow direct spectrophotometric determination without chemical modification **(Figure 2)**. Most reported methods use aqueous buffers or mild acidic/alkaline solutions, though some procedures employ organic solvents such as methanol or chloroform. The ability to avoid derivatization steps gives Etoricoxib a natural advantage in greenness compared to Pregabalin.

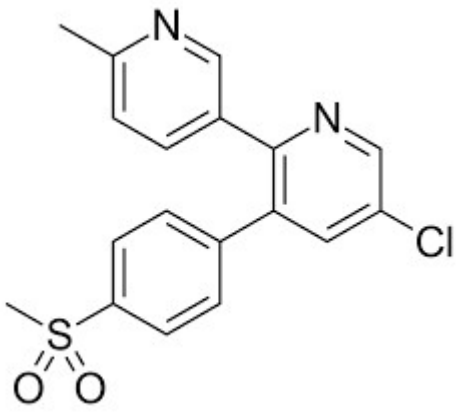


Figure 2: Chemical structure of Etoricoxib

Rationale for Comparative Assessment

Both Pregabalin and Etoricoxib are widely prescribed drugs that require routine quality control in bulk and pharmaceutical dosage forms. Their **contrasting molecular properties** — Pregabalin lacking chromophores (necessitating derivatization) and Etoricoxib having strong intrinsic absorbance (allowing direct methods) — make them an ideal pair for a **comparative greenness assessment**. By applying AGREE and GAPI, this review highlights not only the environmental impact of UV spectrophotometric methods for these drugs but also pathways for more sustainable analytical development.

2. GREEN ANALYTICAL CHEMISTRY (GAC) AND GREEN METRICS

The concept of Green Analytical Chemistry (GAC) was formally introduced in 2000 as an extension of the twelve principles of green chemistry proposed by Anastas and Warner in 1998 **[18]**. While these principles were originally developed for synthetic chemistry, they were later adapted to the field of analytical sciences to minimize the environmental impact of testing and quality control procedures. The fundamental aim of GAC is to ensure that analytical methods remain accurate, reliable, and reproducible, while also being environmentally sustainable. The central challenge in implementing GAC lies in balancing high analytical performance with a low environmental burden. Analytical procedures must provide adequate sensitivity, selectivity, and reproducibility, yet also reduce reagent consumption, minimize waste, and conserve energy. To achieve this, the original twelve principles of green chemistry were modified into a framework tailored for analytical chemistry. These principles highlight the importance of direct analysis with minimal sample preparation, the reduction of sample size and number of analyses, the preference for in situ measurements, and the application of automation and miniaturization. They further emphasize the avoidance of derivatization, the prevention and minimization of waste, the selection of safer solvents and auxiliaries, the use of energy-efficient instrumentation, the introduction of renewable reagents, the development of multi-analyte methods, and the improvement of operator safety, all of which ultimately contribute to reducing the overall environmental impact of analytical processes **[19, 20]**.

To evaluate the degree to which analytical methods comply with these principles, a number of greenness metrics have been developed. Among the most recognized are the National Environmental Methods Index

(NEMI), the Analytical Eco-scale, the Green Analytical Procedure Index (GAPI), and the Analytical GREEnness Metric (AGREE) **[21–23]**. Of these, GAPI and AGREE have emerged as the most comprehensive and widely used assessment tools.

The Green Analytical Procedure Index (GAPI), introduced in 2018, evaluates the environmental impact of an analytical method across its entire workflow. It is represented graphically as a pictogram consisting of fifteen fields that correspond to sampling, sample preparation, reagents and chemicals, instrumentation, and waste management. Each field is color-coded to reflect its environmental impact, with green indicating favorable conditions, yellow reflecting moderate impact, and red denoting unfavorable practices. In this way, GAPI provides a stage-by-stage visualization of the strengths and weaknesses of a method in relation to sustainability **[21]**.

The Analytical GREEnness Metric (AGREE), developed in 2020, is a software-based tool that aligns directly with the twelve principles of GAC **[22]**. It generates a radial pictogram in the form of a clock face, with each segment corresponding to one of the principles, and produces a single numerical score ranging from 0, indicating poor compliance, to 1, indicating excellent greenness.

The software also allows weighted scoring so that specific principles, such as solvent safety or waste minimization, may be prioritized depending on the user's objectives. AGREE therefore provides a clear, quantitative evaluation of overall greenness, while GAPI complements it by pinpointing environmentally critical steps within the workflow. The combined application of these two tools thus offers a robust and comprehensive assessment of the sustainability of analytical procedures **[23]**.

3. METHODOLOGICAL TRENDS IN UV SPECTROPHOTOMETRY

3.1 Pregabalin

Pregabalin presents a particular challenge in UV spectrophotometric analysis because its molecular structure lacks strong chromophores. This absence of intrinsic absorbance in the UV region necessitates the use of derivatization to generate measurable chromophoric groups. Reported methods therefore rely on a variety of chromogenic reagents, including DNPH, MBTH, Gibb's reagent, vanillin, benzoyl chloride, ninhydrin, and ascorbic acid in combination with salicylaldehyde **[1–8]**. These reagents introduce additional complexity into the analytical workflow and often require the use of organic solvents such as methanol or dimethylformamide (DMF), both of which

contribute significantly to chemical hazard and environmental burden.

Most procedures generate between 5 and 10 mL of solvent waste per analysis. While this amount is relatively modest compared with separation-based techniques, it remains less than ideal when considered under the principles of GAC. Energy consumption is generally low, since UV spectrophotometry is less resource-intensive than chromatographic or mass spectrometric methods. Nevertheless, the fundamental drawback of these procedures lies in the derivatization step itself. Derivatization not only increases reagent consumption and lengthens analysis time but also reduces the overall greenness profile of the method. Although Pregabalin assays provide adequate sensitivity and specificity, their reliance on hazardous solvents and derivatization reagents prevents them from achieving higher levels of environmental sustainability. These findings are summarized in **Table 1**, which outlines the compliance of Pregabalin procedures with each of the twelve AGREE principles.

3.2 Etoricoxib

Etoricoxib, in contrast, possesses extended aromatic and heteroaromatic systems that confer strong intrinsic UV absorbance in the range of 233 to 301 nm. This structural feature permits direct spectrophotometric quantification without the need for chemical modification, providing a significant advantage in terms of method simplicity and environmental compatibility. The majority of reported Etoricoxib methods therefore involve direct UV absorbance at characteristic wavelengths, which eliminates the need for derivatization and shortens the analytical process **[9–15]**. The detailed evaluation against the twelve principles is presented in **Table 2**, which demonstrates the advantages of Etoricoxib over Pregabalin in terms of sustainability.

Table 1: AGREE Principles Evaluation – UV–Vis Spectrophotometric Methods for Pregabalin

Parameter	Method 1	Method 2	Method 3	Method 4	Method 5	Method 6	Method 7	Method 8
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	Infield sampling and online analysis
Minimal Sample Size	100 mg	100 mg	100 mg	75 mg	25 mg	75 mg	25 mg	40 mg
In-situ Measurements	On-line	On-line	On-line	On-line	On-line	On-line	On-line	On-line
Integration of Analytical Processes	3 or fewer steps	3 or fewer steps	3 or fewer steps	3 or fewer steps	3 or fewer steps	3 or fewer steps	3 or fewer steps	3 or fewer steps
Automation & Miniaturization	Semi-automatic, not miniaturized	Semi-automatic, not miniaturized	Semi-automatic, not miniaturized	Semi-automatic, not miniaturized	Semi-automatic, not miniaturized	Semi-automatic, not miniaturized	Semi-automatic, not miniaturized	Semi-automatic, not miniaturized
Derivatization	Yes (DNPH)	Yes (Vanillin)	Yes (Sodium Nitroprusside)	Yes (Gibb's reagent)	Yes (MBTH reagent)	Yes (Benzoylation)	Yes (AA & Salicylaldehyde)	Yes (Ninhydrin)
Minimization of Waste	~10 mL	~5–10 mL	~5–10 mL	~5–10 mL	~5–10 mL	~5–10 mL	~10 mL	~5–10 mL
Number of Analytes Determined	1	1	1	1	1	1	1	1
Energy Use Minimization	~0.1 kWh/analysis	~0.1 kWh/analysis	~0.1 kWh/analysis	<0.1 kWh/analysis	<0.1 kWh/analysis	<0.1 kWh/analysis	~0.1 kWh/analysis	<0.1 kWh/analysis
Use of Renewable Reagents	Not Biobased	Biobased	Not Biobased	Not Biobased	Not Biobased	Not Biobased	Not Biobased	Not Biobased
Elimination / Replacement of Toxic Reagents	No (methanol & DNPH)	Yes (low toxicity)	No (toxic reagent)	No (hazardous reagent)	No (hazardous reagent)	No (methanol & reagents)	No (methanol & DMF)	No (methanol & ninhydrin)
Operator Safety	Toxic to aquatic life, highly flammable, corrosive	Low hazard	Toxic to aquatic life	Toxic to aquatic life, irritant	Toxic to aquatic life, irritant	Corrosive, flammable	Flammable & toxic solvents	Toxic to aquatic life, flammable, irritant
Reference	1	2	3	4	5	6	7	8

Table 2: AGREE Principles Evaluation – UV–Vis Spectrophotometric Methods for Etoricoxib

Parameter	Method 1	Method 2	Method 3	Method 4	Method 5	Method 6	Method 7
Sampling Procedure	In-field sampling and on-line analysis	In-field sampling and on-line analysis	In-field sampling and on-line analysis	In-field sampling and on-line analysis	In-field sampling and on-line analysis	In-field sampling and on-line analysis	In-field sampling and on-line analysis
Amount of Sample (mg)	60 mg	60 mg	60 mg	10 mg	100 mg	60 mg	100 mg
Positioning of Analytical Device	On-line	On-line	On-line	On-line	On-line	On-line	On-line
Steps in Sample Preparation	3 or fewer steps	3 or fewer steps	3 or fewer steps	3 or fewer steps	3 or fewer steps	3 or fewer steps	3 or fewer steps
Automation & Sample Size	Semi-automatic; not miniaturized	Semi-automatic; not miniaturized	Semi-automatic; not miniaturized	Semi-automatic; not miniaturized	Semi-automatic; not miniaturized	Semi-automatic; not miniaturized	Semi-automatic; not miniaturized
Derivatization	None	None	None	None	None	Yes	None
Analytical Waste	~50 mL	~50 mL	~50 mL	~10–15 mL	~10 mL	~10 mL	~10 mL
No. of Analytes Determined	1	2	2	1	1	1	1
Energy Use	~0.1 kWh/sample	~0.1 kWh/sample	~0.1 kWh/sample	<0.1 kWh/sample	<0.1 kWh/sample	<0.1 kWh/sample	<0.1 kWh/sample
Reagents Renewable?	No	No	No	No	No	No	No
Toxic Reagents	No	No	No	Yes (HCl)	Yes (methanol)	Yes (chloroform, organics)	Yes (methanol)
Operator Safety Threats	Low hazard	Mild irritant	Mild irritant	Corrosive	Flammable, toxic	Toxic, harmful, flammable	Flammable (vapors)
References	9	10	11	12	13	14	15

These procedures commonly employ aqueous buffers, mild acidic or alkaline solutions, and in some cases organic solvents such as methanol or chloroform. Waste volumes are slightly higher than those reported for Pregabalin, typically between 10 and 15 mL per analysis, but this increase is offset by the use of less hazardous aqueous solvents in most methods. Energy demands are minimal, as in the case of Pregabalin, due to the inherent efficiency of UV spectrophotometric instrumentation. The absence of derivatization not only reduces chemical use and waste but also improves compliance with the principles of GAC.

Taken together, Etoricoxib methods demonstrate a stronger alignment with GAC principles than Pregabalin methods. Their reliance on direct analysis, simpler solvent systems, and reduced chemical modification provides a natural greenness advantage, reinforcing the role of molecular structure in determining the environmental sustainability of spectrophotometric procedures.

4. GREENNESS ASSESSMENT RESULTS

4.1 AGREE

The AGREE tool provided a quantitative overview of the greenness of the reported UV spectrophotometric methods. For Pregabalin **[1–8]**, the AGREE scores ranged between 0.61 and 0.74. These values indicate moderate greenness, with the variation largely attributed to the type of derivatization reagent employed. Methods that relied on hazardous chromogenic agents such as DNPH and MBTH consistently produced lower scores, whereas those using relatively benign reagents such as vanillin or ascorbic acid achieved higher values within the range. The numerical outcomes therefore highlight the critical role of reagent selection in shaping the environmental profile of Pregabalin analysis.

Etoricoxib methods **[9–15]** demonstrated more consistent performance, with AGREE scores spanning a narrower range of 0.65 to 0.71. The highest scores were obtained for direct UV procedures employing aqueous or mildly acidic and alkaline solvents, while methods incorporating organic solvents such as methanol or chloroform achieved comparatively lower values. Overall, AGREE confirmed that Etoricoxib methods are inherently greener than those of Pregabalin, largely due to the structural advantage of direct UV absorbance that eliminates the need for derivatization.

4.2 GAPI

The GAPI tool complemented AGREE by providing a stage-by-stage visualization of each method's workflow. For Pregabalin, GAPI pictograms were consistently marked by red fields in sample preparation and

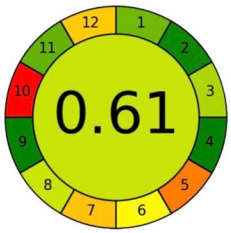
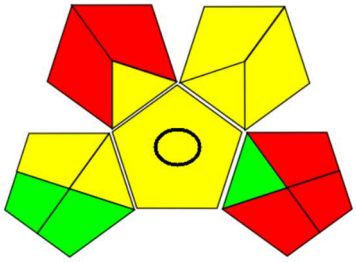
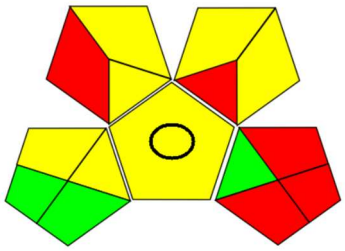
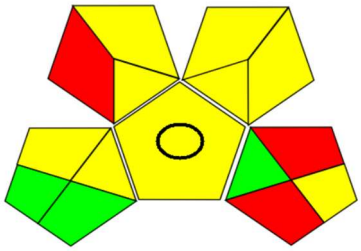
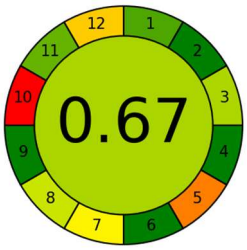
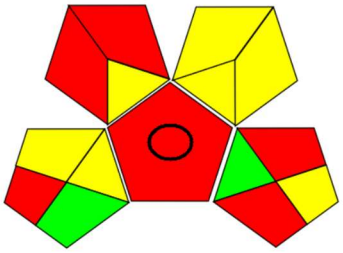
reagent categories, reflecting the environmental burden of derivatization and the use of toxic solvents such as methanol and DMF. Yellow fields were observed in waste generation, which typically ranged from 5 to 10 mL per analysis, and in automation, since most reported methods were not miniaturized. Green fields predominated in the instrumentation stage, consistent with the low energy requirements of UV spectrophotometry. Collectively, these outcomes indicated that the unavoidable need for derivatization remains the central limitation in enhancing the greenness of Pregabalin methods.

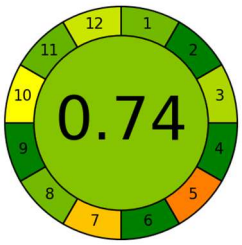
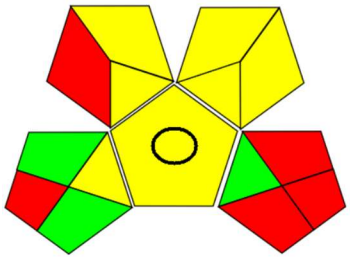
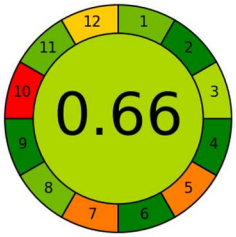
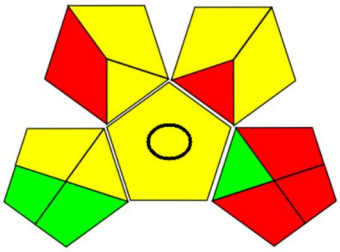
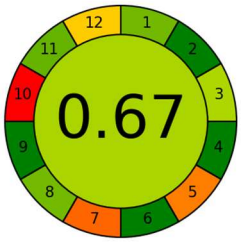
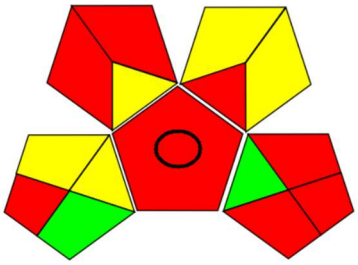
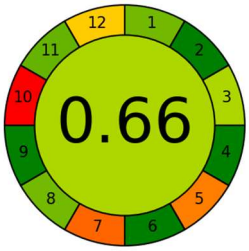
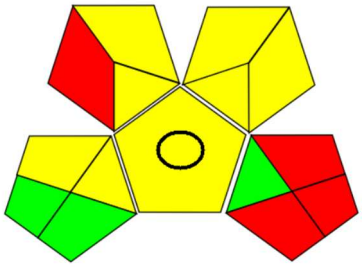
For Etoricoxib, GAPI pictograms were more favorable. Green fields were frequently observed in sample preparation, owing to the feasibility of direct UV analysis, as well as in reagents and instrumentation, particularly when aqueous solvents were used. Yellow fields were associated with waste volumes of 10 to 15 mL and with the use of mildly acidic or alkaline solvents. Red fields were relatively rare and occurred only in methods that employed hazardous organic solvents such as chloroform. Taken together, the GAPI assessments confirmed that Etoricoxib methods exhibit greater alignment with the principles of GAC compared to Pregabalin, with direct analysis and reduced solvent hazard serving as key strengths. The combined outcomes of AGREE and GAPI for all eight reported Pregabalin methods are summarized in **Table 3**. The consolidated AGREE and GAPI results for Etoricoxib are presented in **Table 4**.

4.3 Comparative Interpretation

When considered together, the results from AGREE and GAPI provide a clear comparative perspective. Pregabalin methods displayed greater variability in greenness because of their dependence on derivatization and the diversity of reagents employed. Even the best-performing methods remained limited by the absence of direct analysis. In contrast, Etoricoxib methods demonstrated consistent greenness, particularly those relying on direct UV determination with aqueous solvents. Despite these differences, both drug classes shared common shortcomings, including the absence of renewable reagents, the lack of miniaturized or automated systems, and the generation of moderate amounts of solvent waste. These findings emphasize the need for methodological innovation to bridge the gap between analytical performance and environmental sustainability. The combined AGREE and GAPI results for both drugs are synthesized in **Table 5**, which clearly highlights derivatization as the major barrier to greenness in Pregabalin methods and solvent selection as the main limitation in Etoricoxib procedures.

Table 3: AGREE and GAPI Assessment – Pregabalin

Method No.	AGREE Score / Image	GAPI Score / Image
1		
2		
3		
4		

5		
6		
7		
8		

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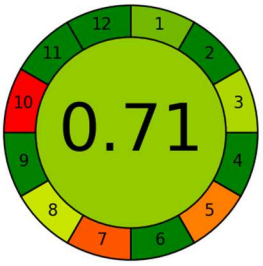
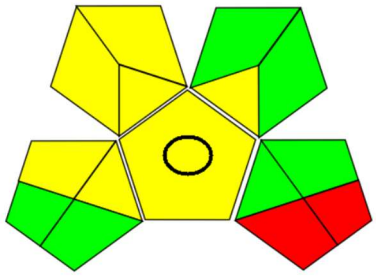
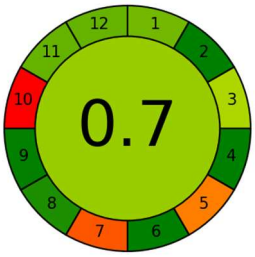
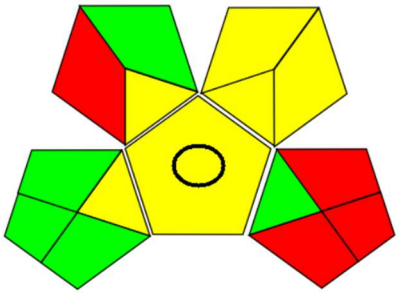
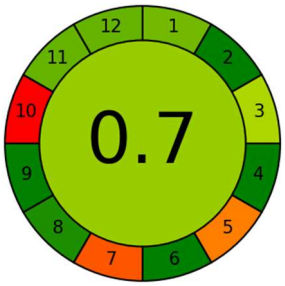
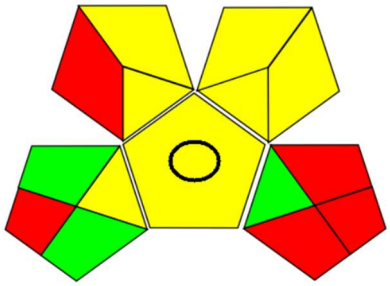
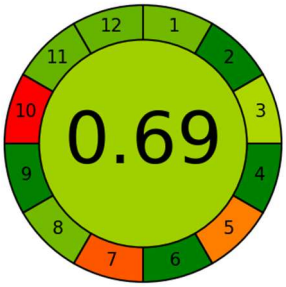
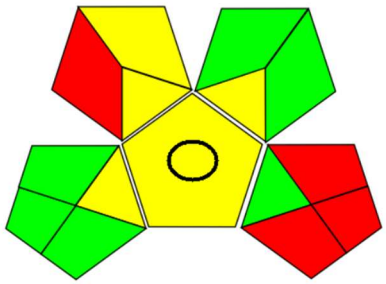
Method No.	AGREE Score / Image	GAPI Score / Image
1		
2		
3		
4		

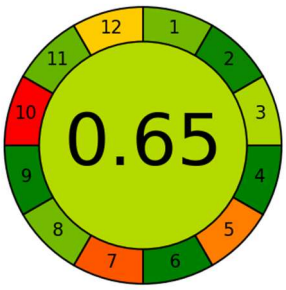
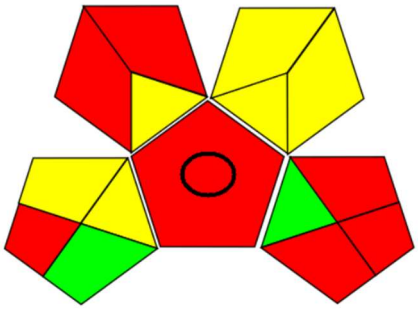
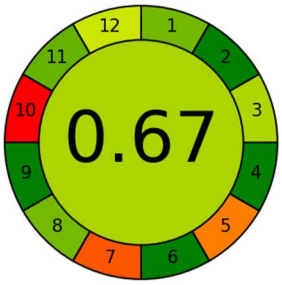
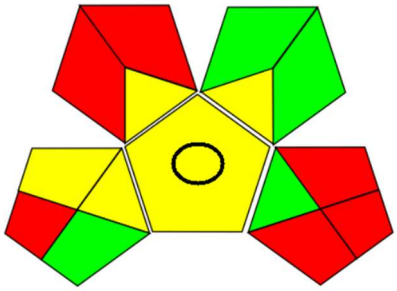
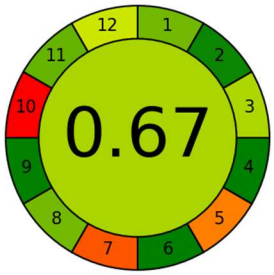
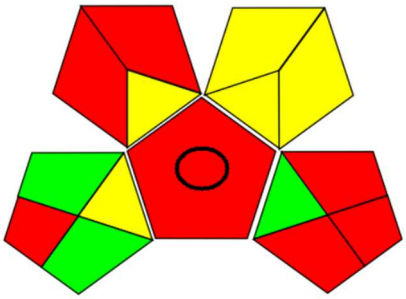
5		
6		
7		

Table 5: Comparative Summary

Feature	Pregabalin	Etoricoxib
Derivatization	**Essential**	**Rare / not required**
Solvents	**Methanol, DMF, hazardous organics**	**Mostly aqueous, mild acid/base, some organics**
Waste	**5–10 mL**	**10–15 mL**
Renewable reagents	**Absent**	**Absent**
AGREE scores	**0.61–0.74**	**0.65–0.71**
GAPI profile	**Multiple red zones (derivatization, solvents)**	**Mostly green/yellow; red only for organics**
Overall greenness	**Moderate, variable**	**Moderate–High, consistent**

5. DISCUSSION

The comparative greenness evaluation of Pregabalin and Etoricoxib UV spectrophotometric methods illustrates how the structural characteristics of drug molecules influence the sustainability of their analytical procedures. Pregabalin, owing to the absence of intrinsic chromophores, cannot be quantified directly by UV spectrophotometry. This limitation necessitates derivatization with chromogenic reagents, which, although effective for detection, introduces additional steps, hazardous chemicals, and solvent use. The consequence of this is evident in the AGREE scores, which ranged from 0.61 to 0.74 across reported methods. Lower scores were associated with derivatization using toxic reagents such as DNPH and MBTH, while methods employing comparatively safer reagents such as vanillin or ascorbic acid achieved higher values within the range. GAPI pictograms confirmed this trend, consistently highlighting red zones in sample preparation and reagent categories, while instrumentation fields remained green due to the inherent energy efficiency of UV spectrophotometry. Thus, although Pregabalin methods can be moderately green, derivatization remains the critical factor limiting their sustainability.

In contrast, Etoricoxib possesses aromatic and heteroaromatic structures that confer strong UV absorbance, enabling direct spectrophotometric determination without chemical modification. This structural advantage is reflected in its AGREE scores, which remained within a narrow range of 0.65 to 0.71, indicating consistent greenness across different reported methods. The best scores were obtained for procedures based on aqueous or mildly acidic/alkaline solvents, while lower scores were associated with methods utilizing organic solvents such as methanol or chloroform. GAPI pictograms for Etoricoxib largely displayed green fields in sample preparation and instrumentation, with yellow zones associated with moderate waste volumes (10–15 mL per analysis). Red zones were relatively uncommon and limited to methods involving hazardous organic solvents. Compared to Pregabalin, Etoricoxib methods therefore demonstrated greater alignment with the principles of GAC, primarily due to their ability to avoid derivatization.

Taken together, the findings highlight a clear distinction between the two drugs. Pregabalin methods are hindered by structural limitations that necessitate derivatization, leading to greater variability and reliance on hazardous reagents. Etoricoxib methods, on the other hand, benefit from direct UV absorbance,

allowing consistent and greener procedures. Both sets of methods, however, share common drawbacks such as the absence of renewable reagents, lack of miniaturization or automation, and generation of moderate solvent waste.

The complementary use of AGREE and GAPI proved valuable in this comparative assessment. While AGREE provided a clear numerical distinction between methods, GAPI offered a workflow-based visualization that pinpointed specific environmental concerns, particularly derivatization in Pregabalin and organic solvent use in Etoricoxib. The combined insights reinforce the need for future UV spectrophotometric methods to adopt derivatization-free approaches where possible, prioritize safer aqueous solvents, and integrate greenness assessment as part of standard method validation.

6. CONCLUSION

This review highlights the importance of applying green analytical chemistry principles to routine pharmaceutical analysis by comparing UV spectrophotometric methods reported for Pregabalin and Etoricoxib. The findings demonstrate that molecular structure plays a decisive role in determining the greenness of analytical procedures. Pregabalin, which lacks intrinsic chromophores, requires derivatization with chromogenic reagents. This necessity results in greater chemical consumption, the use of hazardous solvents, and reduced sustainability, as reflected in AGREE scores ranging between 0.61 and 0.74 and GAPI pictograms consistently marked by red zones in sample preparation and reagent use. Etoricoxib, in contrast, benefits from its strong intrinsic UV absorbance, which permits direct determination without derivatization. Consequently, its reported methods showed higher consistency, with AGREE scores between 0.65 and 0.71 and GAPI profiles dominated by green and yellow fields, with red zones limited to occasional use of organic solvents.

The comparative evaluation establishes that Etoricoxib methods are generally more aligned with the principles of green analytical chemistry than those for Pregabalin. Nonetheless, both drugs' methods share common limitations, including moderate solvent waste, absence of renewable reagents, and lack of miniaturization or automation. To enhance sustainability, future UV spectrophotometric methods should aim to eliminate derivatization in Pregabalin analysis, fully replace hazardous solvents with aqueous alternatives in Etoricoxib procedures, and integrate greenness metrics such as AGREE and GAPI alongside ICH validation

parameters. Incorporating these considerations will not only improve environmental performance but also set new standards for sustainable pharmaceutical quality control.

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