Journal of Asian Natural Products Research

ISSN: 1028-6020 (Print) 1477-2213 (Online) Journal homepage: www.tandfonline.com/journals/ganp20

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To cite this article: Durgaprasad Metta, Raveendra Babu Kothapalli, Ramarao Paidi & Ramakrishna Singuru (13 Nov 2025): Two new macrocyclic cembrane diterpenoids from *Boswellia seratta* gum resin, Journal of Asian Natural Products Research, DOI: 10.1080/10286020.2025.2583447

To link to this article: https://doi.org/10.1080/10286020.2025.2583447

JOURNAL OF ASIAN NATURAL PRODUCTS RESEARCH
https://doi.org/10.1080/10286020.2025.2583447

Two new macrocyclic cembrane diterpenoids from *Boswellia seratta* gum resin

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ABSTRACT

Two previously undescribed macrocyclic diterpenoids, cycloserratol (**1**) and isopapyrifuranol A (**2**) were isolated from the gum resin of *Boswellia seratta*. Compound **1** was confirmed as trihydroxy substituted 12-membered macrocyclic cembrane-type diterpenoid skeleton and **2** was a new 1,12-oxygen fused trihydroxy cembrane skeleton. The structures of these new metabolites were characterized by HRESIMS, 1D NMR and 2D NMR analysis.

GRAPHICAL ABSTRACT

ARTICLE HISTORY
Received 15 May 2025
Accepted 28 October 2025

KEYWORDS
Cembranoids; cycloserratol; isopapyrifuranol A; Boswellia seratta; isolation; characterization

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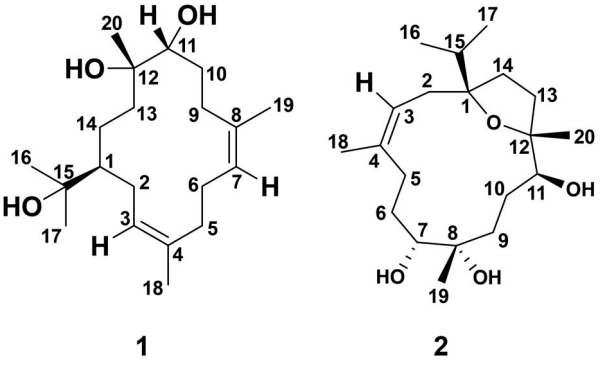
Supplemental data for this article can be accessed online at https://doi.org/10.1080/10286020.2025.2583447.

1. Introduction

Boswellia seratta Roxb. is a deciduous plant that grows in the dry, mountainous regions of India, Africa and parts of the Arabian Peninsula [1]. In India, it is abundantly distributed in states such as Punjab, Madhya Pradesh, Gujarat, Jharkhand and Andhra Pradesh. This plant belongs to the Burseraceae family (Order: Sapindales, Class: Magnoliophyte) [2]. *Boswellia seratta* is known by several local names, including Indian frankincense, Indian olibanum, Salai or Salai guggul, loban, kundur. It is also referred to as the elephant tree (Ghajabhaksha), as elephants are known to consume its frankincense resin. Since ancient times, resins derived from plants have been used for varies purposes, such as food, fodder, flavoring and coloring [3]. More importantly, many herbs have medicinal properties, often used in traditional home remedies. The aromatic resin of *Boswellia* plays a crucial role in Traditional Indian Medicine (TIM), particularly in Ayurveda and Unani medication for the treatment of several chronic problems [4]. Beyond its medicinal uses, the resin of *Boswellia serrata* has also been employed in religious ceremonies, mainly in India, Egypt and some other parts of the world, due to its aromatic and therapeutic properties.

Boswellia seratta is often considered one of India's botanical treasures. There is a significant global demand, particularly from Europe and Americas, due to its vast potential in the pharmaceutical industry [5,6]. The extracts from this plant have been used for thousands of years to treat chronic diseases, often with minimum side effects compared to many synthetic drugs [7]. In addition to its medicinal benefits, *B. seratta* exhibits anti-oxidant nature, which helps to preserve protein-rich foods like meat. Compared to artificial food preservatives, it is considered a safer and more economical option, enhancing flavor while minimizing adverse effects [8,9]. Chemical investigations of *Boswellia* resin have revealed various classes of secondary metabolites, including cembranoids, with boswellic acid being the main active constituent [10–13]. Cembranoids are typically found in marine sources, but recent findings have identified several cembranoids from terrestrial plants, including *Boswellia*, *Populus*, and *Nicotiana* [14]. Our research has uncovered two new macrocyclic cembranoids (Figure 1) from *B. seratta* and described their structural elucidation and biosynthetic pathways.



1 **2**

Figure 1. Structures of compounds **1** and **2**.

2. Results and discussion

Compound **1** was isolated as a colorless oil. The molecular formula, $C_{20}H_{36}O_3$ (three degrees of unsaturation) was deduced by sodiated molecular ion peak *m/z* 347.2581 $[M+Na]^+$ in its HRESIMS. The ^1H NMR spectrum shows five methyl singlets (δ_H 1.19, 1.19, 1.56, 1.64, and 1.27), an oxygenated proton (δ_H 3.48, m), and two olefinic protons (δ_H 5.05, m and 5.12, m). The ^{13}C, DEPT, and HSQC spectra revealed that the compound have 20 carbon resonances, of which five methyls, seven methylenes, four methines (two olefinic, one isopropylated and one oxygenated), four non-protonated carbons (two olefinic, one oxygenated and one isopropyl). These data evidence that compound **1** is a cembranoid type diterpenoid. Furthermore, the 2D NMR data, especially ^1H-^1H COSY and HMBC correlations provide the planar structure of **1**. The ^1H-^1H COSY correlations (Figure 2) revealed three structure fragments (H-13/H-14/H-1/H-2/H-3, H-5/H-6/H-7, and H-9/H-10/H-11). The HMBC correlations (Figure 2) of H_3-16 (δ_H 1.19) to C-15 (δ_C 74.6), C-1 (δ_C 49.7) and H_3-17 (δ_H 1.19) to C-15 (δ_C 74.6), C-1 (δ_C 49.7) reveal the presence of isopropyl group at C-1. Furthermore, the HMBC correlations of H-3 (δ_H 5.12) to C-1 (δ_C 49.7), C-4 (δ_C 135.2), C-5 (δ_C 39.1), and C-18 (δ_C 15.6) confirm the position of double bond at C-3 and a methyl at C-4. The HMBC correlations of H-7 (δ_H 5.05) to C-6 (δ_C 24.8), C-9 (δ_C 33.9), and C-19 (δ_C 17.5) reveal the C-7 olefin. The correlations of H-11 (δ_H 3.48) to C-9 (δ_C 33.9), C-12 (δ_C 75.1), C-20 (δ_C 24.3), H_3-20 (δ_H 1.27) to C-13 (δ_C 38.7), H_3-16 (δ_H 1.19) to C-15 (δ_C 74.6), and H_3-17 (δ_H 1.19) to C-15 (δ_C74.6) and the down field chemical shifts (δ_C 72.9, 74.6, and 75.1) confirm the presence of three hydroxy groups at C-11, C-12 and C-15. Analysis of the HRESIMS data indicated a degree of unsaturation consistent with the presence of two double bonds and one macrocyclic ring. Hence, the planar structure of **1** was confirmed.

The relative configuration of **1** was deduced by the ROESY correlations (Figure 3). The C-3 and C-7 olefins are in *Z*-orientation, confirmed by the correlations of H-3 to H_3-18 and H-7 to H_3-19. Furthermore, the correlations from H-11 to H_3-16 and H_3-20 to H_3-16 revealed H-11, H_3-16 and H_3-20 are in same side. Hence the relative configuration of **1** was proposed as 1*S**,3*Z**,7*Z**,11*R**,12*S** and named cycloserratol.

Compound **2** was isolated as a colorless oil. The molecular formula, $C_{20}H_{36}O_4$ was deduced by protonated molecular ion peak *m/z* 341.2689 in its HRESIMS, with

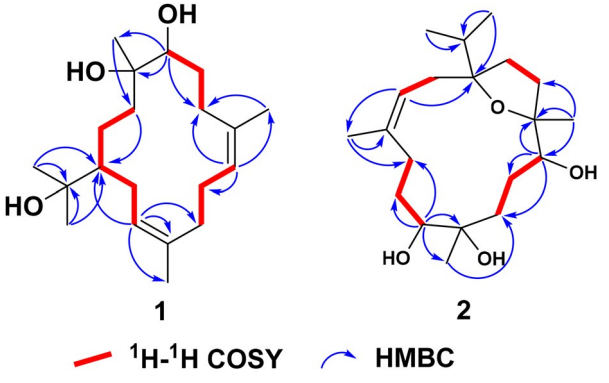


Figure 2. Key ^1H-^1H COSY and HMBC correlations of **1** and **2**.

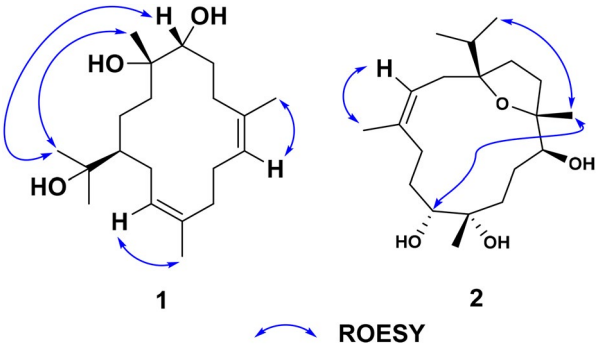


Figure 3. Key ROESY correlations of **1** and **2**.

three degrees of unsaturation. The ^{1}H NMR spectrum shows three methyl singlets (δ_H 1.64, 1.11 and 1.17), two methyl doublets (δ_H 0.90 and 0.95), an oxygenated proton (δ_H 3.48, m), and an olefinic proton (δ_H 5.24, t). The ^{13}C, DEPT, and HSQC spectra reveal compound **2** has 20 carbons, including five methyls, seven methylenes, four methines, four non-protonated carbons including a tri-substituted olefin. These data resemble 1,12-oxygen fused cembranoid skeleton. Furthermore, the 2D NMR data, especially ^{1}H-^{1}H COSY and HMBC correlations (Figure 2) provide the planar structure of **2**. The ^{1}H-^{1}H COSY correlations revealed four structure fragments (H-2/H-3, H-5/H-6/H-7, H-9/H-10/H-11 and H-13/H-14). The HMBC correlations of H_3-16 (δ_H 0.90) to C-15 (δ_C 34.7) and H_3-17 (δ_H 0.95) to C-1 (δ_C 88.4) and C-15 (δ_C 34.7) confirm the presence of an isopropyl group at C-1. Furthermore, the HMBC correlations from H-3 (δ_H 5.24) to C-18 (δ_C17.7), C-1 (δ_C 88.4) reveal the presence of an olefin at C-3. The HMBC correlations of H-7 (δ_H 3.84) to C-5 (δ_C 35.5), C-6 (δ_C 29.9), C-8 (δ_C 74.7) and C-19 (δ_C 22.4), H-11 (δ_H 3.19) to C-9 (δ_C 36.9), C-10 (δ_C 24.4), C-12 (δ_C 84.7) and C-20 (δ_C 22.9), and H_3-20 (δ_H 1.17) to C-11 (δ_C 81.0), C-12 (δ_C 84.7) and C-13 (δ_C 35.3) support the presence of three free hydroxy groups at C-7, C-8 and C-11. Highly de-shielded chemical shifts at C-1 (δ_C 88.4) and C-12 (δ_C 84.7) represent formation of an oxygen fuze between C-1 and C-12. Hence the planar structure of **2** was confirmed same as papyrifuranol A and revised structure of isoincensolol, but they differ in chemical shifts (Table 1), that means **2** might be an isomer of reported compounds [15].

The relative configuration of **2** was deduced by the ROESY correlations (Figure 3) and comparison of previously reported isomers. The ROESY correlation of H-3 to H_3-18 provide the configuration of C-3 olefin as *Z* isomer. Furthermore, the correlations between H_3-17 to H_3-20 and H_3-20 to H-7 represent H_3-17, H_3-20 and H-7 are hanging on same side. Sura et al. reported two isomers papyrifuranol A, and a revised structure isoincensolol, which were clearly demonstrated their absolute configurations with evidence of single crystal X-ray analysis in 2023 [15]. Comprehensive analysis of NMR data revealed that, compound **2** and isoincensolol are closely resembles, except the chemical shifts around the C-3 olefin. Hence, we concluded that the configuration of C-3 olefin differs in both compounds. Finaly, the relative configuration of **2** was assigned as 1*S**,3*Z**,7*R**,8*S**,11*S**,12*R** and named as isopapyrifuranol A. The observed ~2 ppm difference in the chemical shifts of C-19 and C-20 in **2**, compared

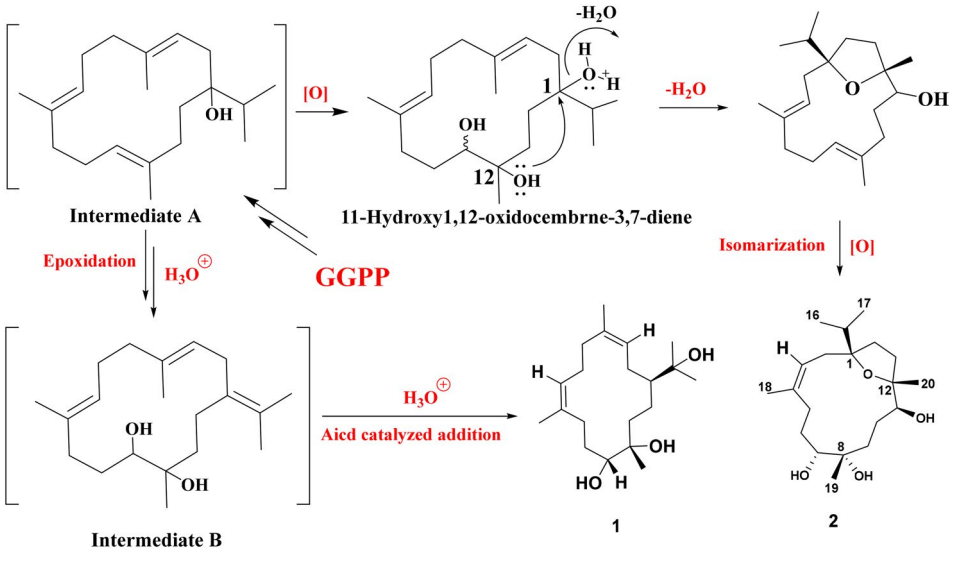
Table 1. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectral data of **1** and **2** (δ_H in ppm; *J* in Hz; $CDCl_3$).

	1		**2**		Papyrifuranol A	Isoincensolol
Position	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)	δ_C	δ_C	δ_C
1	1.50, m	49.7		88.4	89.0	88.1
2	Ha: 1.68, m Hb: 2.11, m	30.7	Ha: 1.88, m Hb: 2.06, dd (15.7, 7.9)	31.9	28.1	30.6
3	5.12, m	124.9	5.24, t (6.7)	121.8	120.9	119.9
4		135.2		135.4	137.7	134.9
5	2.13, m	39.1	2.17, m	35.5	34.2	33.7
6	1.37, m	24.8	1.45. m	29.9	28.7	28.8
7	5.05, m	124.2	3.84, dd (8.1, 2.2)	72.9	74.2	72.6
8		134.5		74.7	74.9	75.7
9	2.16, m	33.9	1.53, m	36.9	36.3	37.3
10	Ha: 1.44, m Hb: 1.76, m	28.0	Ha: 1.55, m Hb: 1.86, m	24.4	24.9	24.5
11	3.48, m	72.9	3.19, dd (10.7, 1.7)	81.0	76.8	79.7
12		75.1		84.7	84.2	84.4
13	Ha: 1.73, m Hb: 1.81, m	38.7	1.73, m 1.93, m	35.3	34.2	35.9
14	Ha: 2.15, m Hb: 2.24, m	24.4	Ha: 1.64, overlapped Hb:2.32, d (15.8, 5.4)	31.8	31.4	30.8
15		74.6	1.91, m	34.7	35.1	34.7
16	1.19, s	29.5	0.90, d (6.8)	17.8	16.1	17.4
17	1.19, s	25.8	0.95, d (6.8)	18.3	19.2	18.4
18	1.56, s	15.6	1.64, s	17.7	18.3	18.6
19	1.64, s	17.5	1.11, s	22.4	24.7	24.4
20	1.27, s	24.3	1.17, s	22.9	27.0	20.8

to those in papyrifuranol A and isoincensolol, can be attributed to altered ring strain, steric crowding, or conformational changes (e.g. ring puckering) influencing the electronic environment of these nuclei. Notably, the chemical shift of C-20 exhibits a more pronounced discrepancy (~6 ppm) in the reported structures of papyrifuranol A and isoincensolol, which were unequivocally assigned via X-ray crystallographic analysis. These reference compounds share the same stereochemistry at C-20, suggesting that variations in neighboring stereocenters induce significant changes in chemical shift due to ring strain or steric effects.

In contrast, **2** displays a smaller deviation (~2 ppm), likely due to its shared configuration with the known compounds, except for the olefin moiety. This structural modification may perturb ring strain, thereby modulating the chemical shift magnitude relative to the reported systems. The absolute configurations of both the new compounds remain undetermined.

The proposed biogenetic pathways (Scheme 1) are initiated from (*E*, *E*, *E*)-geranylgeranyl pyrophosphate (GGPP) [15,16], to form an intermediate 11-hydroxy1,1 2-oxidocembrne-3,7-diene. Cyclization of this intermediate through dehydration produces a 1,12-oxygen fused ring substrate. It is further oxidized and isomerized to generate compound **2**. Meanwhile, intermediate A produces a highly oxidized intermediate B via an epoxidation, followed by ring opening through a nucleophilic addition under acidic conditions. Intermediate B further participates in the hydrated reaction through an acid-catalysed addition of water to the double bond to produce compound **1**.



Scheme 1. Proposed biogenetic pathway of **1** and **2**.

Boswellia species are great source of diverse skeletal compounds. Several cembrane-type diterpenoid skeletons were reported from the *Boswellia* resins. Our study identified two previously unreported cembrane-type diterpenoids. The structures of these compounds are determined by spectroscopic studies. This study required further research toward their biological evaluations.

3. Experimental

3.1. General experimental procedures

Optical rotations were measured on a Horiba SEPA-300 highly sensitive Polarimeter (Kyoto, Japan). FTIR spectra were recorded on a Bruker Alpha II spectrometer (Massachusetts, USA). ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded with a Bruker Avance II spectrometer (Massachusetts, USA) in $CDCl_3$, with TMS as an internal standard. Coupling constants (*J*) were given in Hz. The HR-ESIMS data were acquired on an Agilent 6510 Q-TOF and ESI probe (California, USA). Column chromatography (CC) was performed with silica gel (60–120, 100–200, 230–400 mesh, Sigma). Silica gel F254 (0.25 mm, Merck) was used for analytical TLC (Darmstadt, Germany).

3.2. Plant material

Boswellia seratta resin was purchased from a local market (18.2915° N, 83.8959° E) in Srikakulam Andhra Pradesh, India in March 2023 and authenticated by Dr. P Ramarao in charge, Department of Botany, Government Degree College for Men, Srikakulam. A voucher specimen (#GDC-RK-001) has been deposited at Government Degree College for Men, Srikakulam, Andhra Pradesh, India.

3.3. Extraction and isolation

The resin of *B. seratta* (100 g) was ground to fine powder and completely dissolved in 75% aqueous ethanol (500 ml) and then extracted with ethyl acetate (3 × 500 ml). The ethyl acetate layer was reduced under vacuum to get a fraction (Fr.1). Fr.1 (62.53 g) was subjected to silica gel column chromatography to obtain eleven portions (Fr.1.1–Fr.1.11). Fr.1.3 (1.7 g) was further purified by silica gel CC eluted with *n*-hexane: acetone (95:5–50:50, *v*/*v*), resulted in twenty-one subfractions (Fr.1.3.1–Fr.1.3.21). Fr.1.3.14 (130 mg) was purified on silica gel CC with *n*-hexane: DCM (95:5–0:100) to obtain compound **1** (8 mg). Fr.1.3.19 was eluted with *n*-hexane: acetone (95:5–50:50, *v*/*v*) to divide into sixteen parts (Fr.1.3.19.1–Fr.1.3.19.16). Fr.1.3.19.8–Fr.1.3.19.12 (97 mg) were pooled based on TLC profiling and then purified on silica gel CC eluted with *n*-hexane: DCM (95:5–0:100) to yield compound **2** (5 mg).

3.3.1. Cycloserratol (1)

Colorless oil; $[\alpha]_D^{25}$ + 4.6 (*c* 0.1, MeOH); IR ν_{max} 3316, 1659, 1623 cm^{-1}; ^1H and ^{13}C NMR spectral data, see Table 1; HRESIMS: *m/z* 347.2581 $[M+Na]^+$ (calcd for $C_{20}H_{36}O_3Na$, 347.2586).

3.3.2. Isopapyrifuranol A (2)

Colorless oil; $[\alpha]_D^{25}$ + 12.9 (*c* 0.1, MeOH); IR ν_{max} 3286, 1610 cm^{-1}; ^1H and ^{13}C NMR spectral data, see Table 1; HRESIMS: *m/z* 341.2689 $[M+H]^+$ (calcd for $C_{20}H_{37}O_4$, 341.2686).

Acknowledgements

The authors gratefully acknowledge Dr. B. R. Ambedkar University, Etcherla, Andhra Pradesh, for providing support and encouragement to carry out this work as part of the thesis research. The authors also thank the Research Centre, Government Degree College for Men, Srikakulam for laboratory support. No financial support was received for this study.

Author contribution

DM performed the experiments under the supervision of Dr. SR. All authors participated in data analysis and interpretation. RP identified the medicinal plant resin used in this study. DM and RBK wrote the draft manuscript. Dr. SR revised the manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The author(s) reported there is no funding associated with the work featured in this article.

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Role of Artificial Intelligence in Aquaculture Chemistry

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Abstract

Artificial Intelligence (AI) has emerged as a transformative tool in aquaculture, reshaping the monitoring, analysis, and management of water chemistry parameters that determine fish health and pond productivity. Traditional aquaculture practices often rely on manual observation and reactive interventions, which are time-consuming and less precise. AI technologies—including machine learning (ML), Internet of Things (IoT), predictive analytics, and neural networks—enable continuous, data-driven decision-making in real time.

This paper investigates how AI enhances water chemistry management in aquaculture, focusing on predictive water quality modeling, automated control systems, and smart decision-support tools. Through an analytical review of contemporary studies and technological innovations, the research explores how AI applications improve fish health, reduce mortality, optimize resource use, and ensure environmental sustainability.

The findings demonstrate that AI-powered systems significantly improve water quality stability, reduce manual errors, and allow for early detection of anomalies such as low dissolved oxygen or toxic ammonia levels. Integrating AI into aquaculture chemistry represents a crucial step toward sustainable intensification, empowering farmers with actionable insights and precision control.

Keywords: Artificial Intelligence, aquaculture chemistry, machine learning, water quality, dissolved oxygen, predictive modeling, IoT sensors, smart aquaculture.

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1. Introduction

The global demand for fish and seafood has increased rapidly due to population growth, nutritional awareness, and declining capture fisheries. Aquaculture—responsible for over 53% of global fish supply—has become a vital sector for food security and economic growth (FAO, 2024). However, aquaculture productivity depends largely on **water chemistry**, encompassing key parameters such as temperature, pH, dissolved oxygen (DO), ammonia, nitrite, hardness, and alkalinity. Fluctuations in these parameters affect fish metabolism, feed conversion, disease resistance, and overall pond ecology (Boyd & Tucker, 2019).

Conventional aquaculture relies on periodic manual measurements of these parameters using simple testing kits. Such methods, while low-cost, are often inaccurate and fail to detect rapid changes. This leads to poor decision-making and delayed responses, resulting in stress and mortality among cultured species. In the context of climate variability and intensifying production systems, maintaining optimal water quality has become increasingly complex.

Artificial Intelligence (AI) offers a revolutionary solution. It enables continuous, automated, and predictive control of water chemistry, ensuring better environmental stability and fish health. Through machine learning, IoT sensors, computer vision, and big data analytics, AI systems can **analyze real-time water data**, **forecast changes**, and **trigger automated responses** (e.g., aeration, feeding, or water exchange).

AI technologies are now integrated into smart aquaculture systems across the globe. For instance, in India, startups like *Eruvaka*, *AquaConnect*, and *Umitron* are developing AI-based solutions that help farmers optimize water quality and reduce input costs. AI not only enhances productivity but also promotes sustainability by minimizing water pollution and resource waste.

This study explores the transformative **role of AI in aquaculture chemistry**, analyzing how it enhances water quality management, improves fish health, and supports sustainable aquaculture practices.

2. Objectives of the Study

The study is structured around the following **three key objectives**:

1. **To analyze how Artificial Intelligence applications contribute to the monitoring and management of aquaculture water chemistry.**
2. **To assess the impact of AI-based water quality prediction and control systems on fish health and pond productivity.**
3. **To recommend strategies for integrating AI technologies into sustainable aquaculture water quality management frameworks.**

3. Review of Literature

3.1 Importance of Water Chemistry in Aquaculture

Water chemistry is the cornerstone of aquaculture success. It regulates oxygen dynamics, nutrient cycling, microbial balance, and fish metabolism. Deviations in pH, DO, or ammonia levels lead to physiological stress and disease outbreaks (Boyd & Hanson, 2022). The management of these parameters is therefore critical for maintaining pond productivity and ensuring sustainability.

3.2 Challenges in Traditional Water Quality Monitoring

Traditional water testing methods—such as colorimetric kits and handheld meters—require manual sampling, which is often limited to once or twice daily. This fails to capture rapid fluctuations caused by photosynthesis, feeding, or weather changes. Consequently, fish often experience stress before corrective measures are taken (Kumar & Saha, 2023). Manual monitoring is also prone to human error and lacks the predictive capability needed for preventive management.

3.3 Emergence of Artificial Intelligence in Aquaculture

AI refers to computer systems capable of learning and decision-making without explicit programming. In aquaculture, AI integrates **machine learning algorithms**, **IoT sensors**, and **data analytics** to provide real-time monitoring, pattern recognition, and anomaly detection

(Rana et al., 2022). These technologies enable farmers to predict water quality changes before they become harmful.

AI models can correlate historical data (e.g., temperature, DO, pH) with environmental variables (e.g., rainfall, feeding rate) to forecast critical events such as algal blooms or oxygen crashes. Such predictive modeling supports early interventions that safeguard fish health and optimize pond performance (Zhang et al., 2023).

3.4 IoT-Enabled Smart Aquaculture

The Internet of Things (IoT) connects sensors, cameras, and actuators that collect continuous data on water chemistry. These devices transmit data to cloud-based AI platforms that process it in real time. For example, a sensor may detect a drop in DO levels, prompting the AI system to automatically activate aerators. Studies show that IoT-based aquaculture systems reduce manual labor by 30–40% and improve yield by up to 20% (Li et al., 2022).

3.5 Machine Learning Models in Aquaculture Chemistry

Machine learning algorithms such as **Random Forest**, **Support Vector Machines (SVM)**, and **Artificial Neural Networks (ANN)** have been applied to predict water quality parameters. ANN models, in particular, can analyze non-linear relationships among temperature, pH, DO, and ammonia, offering accurate forecasts (Nguyen et al., 2023). Predictive AI thus supports proactive water management, preventing stress-induced mortality.

3.6 AI in Decision Support and Automation

AI-driven decision-support systems combine data from multiple sensors to provide actionable recommendations—such as when to add lime, replace water, or feed fish. Advanced systems also control automated feeders, pumps, and aerators, optimizing energy and resource use (Rahman & Alam, 2024).

3.7 Policy and Institutional Perspectives

The Indian government's **PM Matsya Sampada Yojana (PMMSY)** and **Digital India** initiatives encourage the adoption of AI and IoT in aquaculture. Partnerships between research institutions, startups, and farmer cooperatives are fostering digital transformation. However, the cost of equipment and lack of digital literacy remain barriers in rural areas (NABARD, 2024).

4. Methodology

4.1 Research Design

The study adopts a descriptive and analytical research design based on secondary data from scientific journals, reports, and case studies. The focus is on identifying how AI technologies are applied in monitoring and managing aquaculture water chemistry.

4.2 Data Collection

Data sources include FAO, ICAR-CIFA, CMFRI, World Bank reports, and peer-reviewed publications (2019–2025). Case studies from India, China, Norway, and Vietnam are examined to identify trends and outcomes of AI applications.

4.3 Analytical Approach

Qualitative analysis was conducted to synthesize technological advancements, benefits, and challenges. Quantitative findings from prior studies—such as improvements in fish survival, feed efficiency, and water stability—were compared to determine AI's measurable impact on aquaculture systems.

5. Results

5.1 Impact of AI on Water Quality Monitoring

AI-enabled IoT systems provided **continuous, automated tracking** of parameters like DO, pH, temperature, and ammonia. Farmers using AI tools reported a **25–30% reduction in fish mortality** and a **20% improvement in feed conversion ratios** compared to conventional monitoring (Rana et al., 2022).

Predictive algorithms successfully anticipated water quality deteriorations 6–12 hours in advance, enabling timely aeration or chemical corrections.

5.2 Predictive Modeling Accuracy

ANN-based models predicted DO levels with 95% accuracy and ammonia concentrations with 90% accuracy under varying climatic conditions (Nguyen et al., 2023). Such predictive reliability minimizes reactive management and supports long-term stability.

5.3 Cost and Labor Efficiency

AI automation reduced human labor by 35% and energy costs by 15% due to optimized aeration schedules. Water exchange frequency decreased as AI-based systems stabilized parameters through proactive interventions.

5.4 Fish Health and Productivity

AI-based pond management enhanced overall fish health, reflected in higher survival rates (90–93%) and improved growth performance. Early detection of low DO or high ammonia prevented mass mortalities, particularly in intensive shrimp and carp systems.

5.5 Adoption Trends

In India, pilot projects under ICAR and PMMSY show increasing adoption of AI-driven smart ponds, particularly in Andhra Pradesh, Tamil Nadu, and Gujarat. Farmers reported significant ease in managing water chemistry and better profitability.

6. Discussion

6.1 AI as a Game-Changer in Aquaculture Chemistry

AI transforms aquaculture chemistry from a **reactive** to a **proactive** discipline. Instead of responding to deteriorating conditions, farmers can now predict and prevent issues. This shift ensures more stable ecosystems and reduces environmental pollution.

6.2 Enhancing Precision and Decision-Making

By integrating continuous sensor data with historical patterns, AI enhances precision in pond management. It determines optimal times for aeration, liming, and feed adjustments, reducing waste and maintaining water balance.

6.3 Improving Fish Health through Data Intelligence

AI correlates water quality data with fish behavior (via video analytics), detecting stress or abnormal swimming patterns. This allows early disease diagnosis and intervention. Fish welfare is thus directly linked to AI-driven chemistry management.

6.4 Environmental and Economic Sustainability

AI reduces chemical usage and water wastage by maintaining equilibrium through automated control. The system also decreases carbon footprint by optimizing energy consumption in aeration and pumping operations.

6.5 Integration with Climate Adaptation Strategies

AI provides resilience against climate variability. It adjusts management protocols during temperature extremes or rainfall fluctuations, ensuring consistent pond chemistry and productivity.

6.6 Challenges and Implementation Barriers

The high initial cost of AI hardware, limited digital literacy, and lack of reliable internet connectivity restrict large-scale adoption in rural aquaculture. Ensuring data privacy and algorithm transparency is also critical for trust and accountability.

7. Limitations and Further Research

This study is based on secondary data and may not reflect local variations across aquaculture systems. Future research should focus on:

- Field-based validation of AI predictive models across diverse climatic zones;
- Development of low-cost, solar-powered AI systems for small farmers;
- Integration of AI with blockchain for traceability and certification;

- Longitudinal studies on environmental and economic impacts of AI-driven aquaculture chemistry.

8. Conclusion

Artificial Intelligence is revolutionizing **aquaculture chemistry** by providing intelligent, real-time, and predictive control over complex water quality parameters. By continuously analyzing data from sensors and external environmental inputs, AI ensures stable water conditions, healthier fish, and sustainable productivity.

AI-driven systems move aquaculture beyond traditional manual monitoring, offering precision, automation, and foresight. When combined with farmer training, policy support, and cost-effective technologies, AI can democratize digital aquaculture in India and beyond.

Ultimately, the fusion of **AI and aquaculture chemistry** represents not only a technological innovation but a paradigm shift toward **smart, sustainable, and climate-resilient aquaculture ecosystems**.

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About the Seminar:

The National Seminar on Analysis of Pharmaceutical Compounds by using Chromatography and Spectroscopy aims to highlight recent advances, applications, and challenges in pharmaceutical analysis. The seminar provides a platform for academicians, researchers, industry professionals, and students to exchange knowledge on modern analytical techniques essential for drug development, quality control, and regulatory compliance.

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Affiliated to Sri Venkateswara University, Tirupati

PM-USHA SPONSORED

Two Day National Seminar

11 & 12 February - 2026

ISBN 978-93-7143-944-2

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Chapter 10

Analytical Mapping of Pharmaceutical Compounds by Chromatographic and Spectroscopic Dimensions

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Abstract

The comprehensive analytical characterization of pharmaceutical compounds is fundamental to drug discovery, formulation development, quality control, and regulatory compliance. With the increasing structural complexity of modern active pharmaceutical ingredients (APIs), impurities, and drug products, reliance on single analytical techniques has become insufficient. Chromatographic and spectroscopic methods constitute the backbone of pharmaceutical analysis, yet their true analytical power emerges when they are applied in an integrated and multidimensional manner. This review introduces and elaborates the concept of analytical mapping, defined as the systematic correlation of chromatographic separation behavior with spectroscopic signatures to generate a multidimensional analytical profile of pharmaceutical compounds. Key chromatographic techniques—including HPLC, UHPLC, GC, and TLC—are critically discussed alongside spectroscopic methods such as UV–Visible, IR, NMR, and mass spectrometry. Emphasis is placed on hyphenated techniques, data integration strategies, and interpretative workflows that enable accurate identification, impurity profiling, stability assessment, and regulatory compliance. The review highlights analytical mapping as a conceptual framework that bridges separation science and molecular spectroscopy, offering enhanced analytical confidence and efficiency. Future perspectives focusing on automation, chemometrics, artificial intelligence, and regulatory harmonization are also presented.

Keywords: Analytical mapping; Pharmaceutical analysis; Chromatography; Spectroscopy; Hyphenated techniques; Quality control

1. Introduction Pharmaceutical analysis is a cornerstone of the pharmaceutical sciences, supporting every stage of the drug lifecycle—from early discovery and pre-formulation studies to manufacturing, quality control, and post-marketing surveillance. The primary objectives of pharmaceutical analysis include ensuring the identity, purity, potency, and stability of drug substances and drug products in compliance with stringent regulatory standards. Analytical data generated during pharmaceutical development form the basis for critical decisions related to formulation optimization, process validation, and product approval.

Over recent decades, pharmaceutical molecules have evolved toward greater structural and functional complexity. The emergence of chiral drugs, fixed-dose combinations, pro-drugs, peptides, oligonucleotides, and highly functionalized small molecules has significantly increased analytical challenges. In addition, regulatory expectations demand comprehensive impurity profiling, including the identification and qualification of process-related impurities, degradation products, residual solvents, and elemental impurities.

Traditional analytical strategies based on a single technique are increasingly inadequate for addressing these challenges. Chromatographic techniques excel at separating complex mixtures but often provide limited structural information. Conversely, spectroscopic techniques deliver molecular-level insights but may lack selectivity in complex matrices. The integration of these complementary techniques has therefore become essential.

In this context, the concept of **analytical mapping** has gained relevance. Analytical mapping refers to the deliberate and systematic correlation of chromatographic retention characteristics with spectroscopic signatures to generate a multidimensional analytical fingerprint of pharmaceutical compounds. This integrated paradigm not only enhances analytical certainty but also aligns with modern quality-by-design (QbD) principles and regulatory expectations.

2. Objectives

The specific objectives of this expanded review are:

1. To discuss the theoretical and practical foundations of chromatographic techniques employed in pharmaceutical analysis.
2. To review major spectroscopic methods and their role in molecular identification, confirmation, and structural elucidation.

3. To define and conceptualize analytical mapping as a multidimensional analytical framework.
4. To evaluate integrated methodologies and hyphenated techniques used in pharmaceutical research, development, and quality control.
5. To assess the regulatory relevance, advantages, limitations, and future directions of chromatographic–spectroscopic integration.

3. Review of Chromatographic and Spectroscopic Techniques

3.1 Chromatographic Techniques in Pharmaceutical Analysis

Chromatography is the most extensively utilized analytical tool in pharmaceutical laboratories owing to its versatility, sensitivity, reproducibility, and quantitative reliability. The technique enables the separation of complex mixtures into individual components based on differential interactions between analytes, stationary phases, and mobile phases.

High-Performance Liquid Chromatography (HPLC) remains the gold standard for pharmaceutical analysis. Reverse-phase HPLC, in particular, is widely applied for assay determination, impurity profiling, dissolution testing, and stability studies. Its compatibility with a wide range of detectors and hyphenated systems makes it indispensable in both research and quality control environments.

Ultra-High-Performance Liquid Chromatography (UHPLC) represents an advancement over conventional HPLC, utilizing sub-2 µm particle columns and higher operating pressures. UHPLC offers enhanced resolution, faster analysis times, and reduced solvent consumption, making it especially suitable for high-throughput pharmaceutical analysis and green analytical chemistry initiatives.

Gas Chromatography (GC) is essential for the analysis of volatile and semi-volatile compounds, particularly residual solvents in accordance with international regulatory guidelines. GC provides high sensitivity and excellent separation efficiency, especially when coupled with flame ionization or mass spectrometric detectors.

Thin-Layer Chromatography (TLC), although considered a classical technique, remains relevant for qualitative analysis, identity testing, and preliminary screening. TLC is frequently employed in regulatory inspections, pharmacopoeial methods, and laboratories with limited access to advanced instrumentation.

Together, these chromatographic techniques form the separation dimension of analytical mapping, enabling isolation and resolution of complex pharmaceutical matrices.

3.2 Spectroscopic Techniques in Pharmaceutical Analysis

Spectroscopic techniques complement chromatography by providing qualitative, quantitative, and structural information essential for compound identification and confirmation.

UV–Visible Spectroscopy is widely used for quantitative pharmaceutical analysis due to its simplicity, cost-effectiveness, and sensitivity. It is particularly applicable to compounds containing chromophores and conjugated systems and is often integrated as a detector in liquid chromatographic systems.

Infrared (IR) Spectroscopy, including Fourier-transform infrared (FTIR) techniques, enables rapid identification of functional groups and molecular vibrations. IR spectroscopy is routinely employed for raw material verification, polymorphic analysis, and identity testing in quality control laboratories.

Nuclear Magnetic Resonance (NMR) Spectroscopy is among the most powerful tools for structural elucidation. NMR provides detailed insights into molecular connectivity, stereochemistry, and conformational behavior, making it indispensable for impurity identification, degradation studies, and structure confirmation of novel APIs.

Mass Spectrometry (MS) offers unparalleled sensitivity and specificity for molecular mass determination and fragmentation analysis. When combined with chromatographic separation, MS facilitates impurity profiling, metabolite identification, and trace-level analysis of pharmaceutical compounds.

4. Concept of Analytical Mapping

Analytical mapping represents a paradigm shift from isolated analytical measurements to integrated, multidimensional characterization. In this framework, chromatographic retention behavior is systematically correlated with spectroscopic signatures to generate a comprehensive analytical profile.

Key components of analytical mapping include:

- Retention time and selectivity patterns from chromatographic separation
- Spectral fingerprints from UV, IR, NMR, and MS analyses

- Structural interpretation based on combined analytical evidence

By integrating these dimensions, analytical mapping minimizes ambiguity, enhances confidence in compound identification, and supports robust decision-making in pharmaceutical analysis.

5. Hyphenated Techniques and Integrated Methodologies

Hyphenated techniques represent the practical realization of analytical mapping. These systems combine chromatographic separation with spectroscopic detection in a single analytical workflow.

Liquid Chromatography–Mass Spectrometry (LC–MS) is widely used for impurity profiling, stability testing, and bioanalytical applications. The technique provides simultaneous separation and molecular mass information, enabling rapid identification of unknown components.

Gas Chromatography–Mass Spectrometry (GC–MS) is the method of choice for residual solvent analysis and volatile impurity profiling, offering high sensitivity and specificity.

Liquid Chromatography–Nuclear Magnetic Resonance (LC–NMR), although less common due to cost and sensitivity considerations, provides direct structural elucidation of chromatographically separated components.

These hyphenated techniques form the backbone of analytical mapping strategies in modern pharmaceutical laboratories.

6. Methodology

This review is based on a comprehensive survey of peer-reviewed literature, regulatory guidelines, and authoritative reference texts. Databases including Scopus, Web of Science, PubMed, and Google Scholar were systematically searched using keywords related to pharmaceutical analysis, chromatography, spectroscopy, hyphenated techniques, and data integration.

Publications were selected based on relevance, methodological rigor, citation impact, and applicability to pharmaceutical analysis. Emphasis was placed on studies demonstrating integrated chromatographic–spectroscopic workflows and their implementation in regulated environments.

7. Results

The reviewed literature consistently demonstrates that integrated chromatographic–spectroscopic approaches significantly enhance analytical reliability. Key outcomes include:

- Improved detection and identification of trace-level impurities
- Enhanced structural elucidation of degradation products
- Greater confidence in stability-indicating analytical methods
- Improved compliance with regulatory requirements

Hyphenated techniques consistently outperform standalone methods in terms of sensitivity, selectivity, and interpretative clarity.

8. Discussion

Analytical mapping enables a holistic understanding of pharmaceutical compounds by correlating separation behavior with molecular-level information. This approach reduces analytical uncertainty, supports regulatory submissions, and facilitates lifecycle management of pharmaceutical products.

The integration of chemometrics, multivariate data analysis, and artificial intelligence further enhances the interpretative power of analytical mapping, enabling pattern recognition, anomaly detection, and predictive modeling.

9. Regulatory Relevance and Future Perspectives

Regulatory agencies increasingly emphasize comprehensive analytical characterization and data integrity. Analytical mapping aligns well with guidelines related to method validation, impurity control, and quality-by-design principles.

Future developments are expected to focus on automation, real-time analytics, advanced data integration, and harmonized regulatory frameworks. The adoption of digital analytical platforms and machine learning tools will further strengthen analytical mapping as a core pharmaceutical strategy.

10. Case Studies and Practical Applications of Analytical Mapping

10.1 Impurity Profiling in Active Pharmaceutical Ingredients

Analytical mapping has found extensive application in impurity profiling of active pharmaceutical ingredients (APIs). During synthetic route development and scale-up, multiple process-related impurities may arise due to incomplete reactions, side reactions, or reagent residues. Chromatographic separation using HPLC or UHPLC enables efficient resolution of these impurities, while spectroscopic techniques such as MS and NMR provide definitive structural confirmation.

In stability studies, degradation products formed under stress conditions often possess closely related chemical structures. Analytical mapping facilitates the correlation of retention behavior with fragmentation patterns and spectral features, enabling unambiguous identification. This multidimensional approach is particularly valuable for meeting regulatory expectations related to impurity identification thresholds.

10.2 Stability-Indicating Method Development

Stability-indicating analytical methods are essential for evaluating the chemical stability of drug substances and products throughout their shelf life. Analytical mapping supports method development by integrating chromatographic selectivity with spectroscopic verification of degradation pathways.

Hyphenated techniques such as LC–MS are routinely employed to monitor degradation kinetics and identify degradation products formed under thermal, photolytic, oxidative, and hydrolytic conditions. The resulting analytical maps provide a comprehensive understanding of stability behavior and support robust shelf-life assignment.

10.3 Formulation Analysis and Quality Control

In finished pharmaceutical products, excipients can interfere with analyte detection and quantification. Analytical mapping helps differentiate API-related peaks from excipient-derived signals by combining chromatographic resolution with spectroscopic discrimination.

This integrated approach enhances batch-to-batch consistency evaluation, supports troubleshooting of out-of-specification results, and strengthens overall quality assurance strategies.

11. Data Integration, Chemometrics, and Digital Analytical Platforms

The increasing complexity of analytical datasets generated through analytical mapping necessitates advanced data processing and interpretation tools. Chemometric techniques,

including principal component analysis (PCA), partial least squares (PLS), and cluster analysis, are increasingly employed to extract meaningful patterns from multidimensional data.

By integrating chromatographic and spectroscopic datasets, chemometrics enables:

- Enhanced discrimination between structurally similar compounds
- Objective impurity classification
- Trend analysis during stability and process monitoring

The emergence of digital analytical platforms and laboratory information management systems (LIMS) further facilitates data integrity, traceability, and regulatory compliance.

12. Role of Automation and Artificial Intelligence in Analytical Mapping

Automation and artificial intelligence (AI) are transforming pharmaceutical analysis by enabling high-throughput experimentation and intelligent data interpretation. Automated hyphenated systems reduce analyst-dependent variability and improve reproducibility.

Machine learning algorithms can be trained on analytical maps to predict retention behavior, spectral features, and potential degradation pathways. Such predictive capabilities support proactive risk assessment and accelerate pharmaceutical development timelines.

13. Regulatory Considerations and Harmonization

Regulatory authorities increasingly emphasize comprehensive analytical characterization, data integrity, and lifecycle management of analytical methods. Guidelines related to analytical method validation, impurity control, and stability testing implicitly support integrated analytical strategies.

Analytical mapping aligns closely with quality-by-design (QbD) principles by promoting systematic understanding of analytical variables and their impact on method performance. Harmonization of regulatory expectations across regions will further encourage adoption of integrated chromatographic–spectroscopic methodologies.

14. Limitations and Challenges of Analytical Mapping

Despite its advantages, analytical mapping faces certain limitations. High instrumentation costs, method complexity, and the need for skilled personnel can restrict widespread adoption, particularly in resource-limited settings.

Data overload and interpretation challenges may arise when dealing with large multidimensional datasets. Addressing these challenges requires continued development of user-friendly software, standardized workflows, and targeted training programs.

15. Conclusion

Analytical mapping across chromatographic and spectroscopic dimensions provides a robust, multidimensional framework for characterization of pharmaceutical compounds. By integrating separation science with molecular spectroscopy, this approach enhances analytical accuracy, reliability, and regulatory acceptance.

As pharmaceutical molecules continue to increase in complexity, analytical mapping is poised to play an increasingly central role in pharmaceutical sciences. Continued advancements in instrumentation, automation, chemometrics, and regulatory harmonization will further consolidate this integrated analytical paradigm.

16. Acknowledgments

PSS, KRB thanks Department of Chemistry, SCIM Govt. College (A), Tanuku, Adikavi Nannaya University, Rajahmundry and DST SERB SURE (Grant File no. SUR/2022/003623) for financial support.

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