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Review Article

CHROMATOGRAPHY AND SPECTROSCOPY TECHNIQUES USED IN THE AUTHENTICATION AND ANALYSIS OF *CANNABIS SATIVA* A MEDICINAL PLANT

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ABSTRACT

Ayurveda uses a variety of bioactive compounds, which are abundant in plants, to cure a variety of diseases. Since ancient times, people have used medicinal herbs, and it's possible to say that this practice is where modern medicine got its start. There is an urgent need for herbal remedies to be assured of both their safety and effectiveness as medicinal plants keep increasing in popularity across the world. With this increasing need, it is very essential that the quality of the herbal medicinal plant must be controlled. In particular, the analysis of medicinal herbs has been around for decades to determine a plant's quality. There are many spectroscopic and chromatographic methods available for analysis, including ultraviolet (UV), Fourier-transform infrared spectrum, NMR spectroscopy or magnetic resonance spectroscopy (MRS), vapor-phase chromatography (VPC), high-pressure liquid chromatography (HPLC) along with mass spectrometry (MS), as well as hyphenated methods like vapor-phase chromatography (VPC)-mass spectrometry, liquid chromatography-hyphenated methods, and liquid chromatography-hyphenated methods. *Cannabis sativa* is a medical plant that is attracting more attention as a result of its strong pharmacological potential and recent changes to the law that permit diverse applications. For phytocannabinoid profiling, it is essential to create analytical techniques that are both time and money effective. The study intends to demonstrate the applicability of methodology for phytocannabinoid profiling of cannabis in addition to explore new analytical approaches in cannabis quality control, including classical spectroscopic as well as chromatographic methods.

Keywords: Medicinal plant, Chromatography, Spectroscopy, *Cannabis sativa*

INTRODUCTION

Since ancient times, most of the aromatic and medicinal plants that can be found across the world today have been used for flavouring food and medication formulations, as well as for their therapeutic and preservation characteristics. For the creation of substitute food additives, there has been a significant increase in interest in recent years for crude extracts as well as the vital oils of culinary and medicinal plants (Al Hashmi *et al.,* 2013).

In Ethiopia and other emerging nations in Asia and Africa, medicinal plants continue to play a significant part in peoples' everyday lives. In addition to enhancing the health as well as security of the local population, medicinal plants supplement or replace contemporary medical therapies, which are frequently insufficiently available (Kuldip *et al.,* 2015). Drugs made from plants are an essential component of Ayurvedic treatment. Both conventional and contemporary medical systems rely on medicinal plants as a supply of basic materials. Herbal remedies and other plant-based products have grown in use and popularity over the past few decades, significantly impacting the healthcare industry (Gavali *et al.,* 2016). Since ancient times, plants have been utilized in folk medicine. The active compounds (alkaloids, flavonoids, glycosides, vitamins, tannins, as well as coumarin compounds) found in plant organs are what give them their medicinal properties. These substances affect the physiological functioning of human as well as animal bodies or operate biologically to combat infections that are responsible for several disorders (Kamkin *et al.,* 2022). Complex plant extracts provide a difficult challenge in terms of separating components, identification plus their quantification. However, a wide range of various separation methods, particular stationary phases, and detectors are now readily available, making it possible to solve practically any separation problem with the necessary selectivity, sensitivity, and speed (Ganzera and Sturm, 2018). Since the beginning of time, tribal people all over the world have routinely used plants and plant-related products as ethnomedicine to cure a variety of illnesses (Agidew, 2022). Traditional medicine was defined by a World Health Organization (WHO) Experts Group as "the complete set of every principle and belief, whether or not, used for the diagnosis, prevention, as well as elimination of physical, mental, and also social imbalances along with depending entirely on firsthand experience and knowledge went verbally or through writing from one generation to the next" (WHO, 1976) (Sofowora *et al.,* 2013). A variety of analytical methods like capillary electrophoresis, gas chromatography or vapor-phase chromatography (VPC), high-pressure liquid chromatography (HPLC), TLC that is thin layer chromatography, and their hyphenated processes to mass spectroscopy (MS), have been used to investigate complex compounds in herbal products. Since LC MS can significantly increase the analytical selectivity as well as sensitivity, it has grown in significance in recent years for the chemical study of Hydroxymethanesulfonate (HMs) (Zhou *et al.,* 2009). The effectiveness of the analytical methodologies affects the plants' performance and safety. Every time we use the analytical procedures, they should be repeatable, accurate, and consistent. In addition to distinct methodologies, drug analysis is listed in many pharmacopeia. For the analysis of plant drugs, Central Council for Research in Ayurvedic Sciences (CCRAS) in India has devised a procedure (Gavali *et al.,* 2016).

I. *Cannabis sativa*:

Cannabis sativa (F. Cannabinaceae) is the scientific name for the annual plant known as cannabis, hashish, or hemp (Kulkarni *et al.,* 2018). Cannabis is included as one of the five sanctified plants in the Atharvana Veda and is described as an origin of joy, happiness,

and even redemption. This is where the first information on cannabis' therapeutic status in India is first documented (Ram *et al.,* 2018). It is likely one of the cultivated plants and has been utilized by humans for many years. It is extensively used and has been around for over 2500 years, according to archaeological findings (Schmidt *et al.,* 2020). Cannabis sativa, generally known as hemp, which is an annual plant with considerable pharmacological relevance that generates secondary cannabis chemicals and other metabolites with therapeutic potential for a number of human health issue (Bowen *et al.,* 2021). Cannabis has been used for medicinal purposes for many years to alleviate a broad range of ailments, including pain, spasms, breathing issues, insomnia, depressed symptoms, and even appetite loss (Mirzamohammad *et al.,* 2021).

The Cannabis genus now contains more than 500 chemicals that are divided into 18 chemical classes. Cannabinoids, also known as terpenophenolics, stand out among these compounds since they are linked to the pharmacological effects of this plant. The most well-known cannabinoids were delta-9-tetrahydrocannabinol (9-THC), a psychoactive cannabinoid, plus cannabidiol (CBD), a psychologically inactive cannabinoid that has recently been widely advocated for medical usage. 9-THC is a key component of the cannabinoids present in *Cannabis sativa* due to its considerable psychoactive effect (Mano-Sousa *et al.,* 2021). Cannabis is being used more and more, thus it's important to have a variety of effective ways for identifying its constituent parts and, in particular, for characterizing the "narcotic compound" (Galand *et al.,* 2004). Over the last ten years, numerous chromatographic procedures with various spectroscopic detection techniques have been used to identify, isolate, and characterize the chemicals in cannabis (Odieka *et al.,* 2022).

Table 1: *Cannabis sativa* L. systematic taxonomy

Division	Angiosperms
Class	Dicotyledons
Subclass	Archichlamydeae
Order	Urticales
Family	Cannabaceae
Genus	*Cannabis*
Species	*sativa* L.

Cannabis analysis is currently an important part of the quality control of plant-based goods used for health and food, as well as for scientific along with legal purposes (Ibrahim *et al.,* 2018; Zampachova *et al.,* 2021). Following are some of the spectroscopic, chromatographic and hyphenated technique analysis for *cannabis sativa* L.

II. Spectroscopic Analysis

Youbin Zheng *et al.,* (2021) discovered that cannabis inflorescence yield along with cannanoid amount i.e concentration did not rise through short-wavelength UV-b radiation, this study found that using UV light as a production technique did not increase cannabis output or the composition of secondary metabolites in inflorescence in any economically significant way.

Michael W. Jenkins *et al.,* (2021) unmasked that during the last phase of blooming at the leaf level *Cannabis sativa L.* responds readily to ultraviolet light with a narrow band, along with blue and red light combined.

In order to determine if combining narrow-bandwidth ultraviolet light with blue and red light over a couple of weeks during blossoming could change the amount of cannabinoids and terpenes without changing the crop's dry weight, gas-exchange parameters, secondary metabolite production, and yield were tested.

Jose Dorado *et al.,* (2001) studied infrared spectroscopic measurement technique for hemp (Cannabis sativa. L) subsequently after specific delignification via Bjerkandera sp. at varying nitrogen levels. In this study, alterations in C/N-modified lignocellulosic substrates of Cannabis sativa L. were discovered using Fourier-transform infrared spectroscopy (FT-IR) during a 7-week solid-state fermenting environment with the white-rot fungus Bjer-kandera spp. strain BOS55.

C.Sanchez Carnerero Callado *et al.,* (2018) reported a comparative study to examine the ability of NIR spectrometer to evaluate THC concentration in Cannabis sativa L. An technique for quantitatively detecting cannabinoids in cannabis raw materials was developed in this work employing near-infrared spectroscopy (NIR) as well as Fourier transform near infrared (FT-NIR) spectroscopy.

Wieland Peschel *et al.,* (2015) reported ^{1}H NMRas well as HPLC with diode array detect (DAD) was used for Cannabis sativa L. chemotype discrimination, extracts profiling, as well as specification. To investigate the applicability of ^{1}H NMRkey signals, four distinct chemotypes were investigated in deuterated dimethyl sulfoxide.

Ada C. Gallo-Molina *et al.,* (2019) reported Tetrahydrocannabinol was extracted, isolated, and isolated from the Cannabis sativa L. plant via supercritical fluid extraction and the solid-phase extraction, the FF can be analyzed using ^{1}H NMRand^{13}C-NMR studies.

Marco Cirrincione *et al.,* (2021) reported and describeda novel high-throughput approach using Fourier transform infrared spectroscopy– attenuated total reflectance (FTIR–ATR) which is a technology developed for determining the kind of fiber in the drug Cannabis sativa L. inflorescences. It is an evidence of concepts for the several chemotypes of the cannabis sativa L.

Francine Gloerfelt-Tarp *et al.,* (2023) developed a chemometric method for cannabinoid measurement based on a global diversity panel for Cannabis sativa L. in which NIRS was able to differentiate between C3-alkyl and C5-alkyl cannabinoids as well as between cannabinoids neutral and acidic form. When paired with chemometrics, the findings show that NIRS has the ability to accurately evaluate cannabis in raw materials.

Luis Ramos-Guerrero *et al.,* (2022) reported Raman microscopy and chemometrics were used to categorize various marijuana strains. The Raman spectrum of five marijuana strains was compared to the conventional cannabinoids THC, CBD, and CBN. Four Cannabis sativa strains (Amnesia Haze, Am-nesiaHy-Pro, Original Amnesia, plus Y Griega) and one Indica strain (Black Domina) were studied.

Stefania Porcu *et al.,* (2022) reported Rapid unchanged Identification of CBD and THC in Cannabis sativa L. employing 1064 nm Raman spectra in which all of the primary Raman modes have been assigned according to the Raman spectroscopy of two distinct cannabis families THC- as well as CBD-rich, 42 naturally obtained samples were analyzed

to get the spectra, as well as a 1064 cm^{-1} excitation wavelength was utilized.

Pedro Henrique P. M. da Silveira *et al.,* (2022) reported the effect of alkaline treatment and graphene oxide coating on the thermal as well as chemical properties of hemp (Cannabis Sativa L.) fibers. In which Hemp fibre (*Cannabis sativa L.*) was subjected to an alkaline treatment before being functionalized with graphene oxide. Chemical, thermal, as well as microstructural characterisation techniques that include Fourier transform infrared and differential scanning calorimetry, TGA which is Thermogravimetric analysis, RAMAN, X-ray diffraction as well as scanning electron microscope were used to investigate this process.

Marcus Daniel Brandbjerg *et al.,* (2023) reported Desorption Electrospray Ionization and MALDI mass spectroscopy imaging were used to look for cannabinoids along with flavonoids within extract of hemp leaves as well as trichomes, in which the cannabinoid CBGA as well as capitate-stalked trichomes have been linked through indirect DESI-MSI tests. In addition to the tiny glandular trichomes, capitate-stalked trichomes also included other cannabinoids, That includes tetrahydrocannabinolic acid (THCA) along with cannabidiolic acid (CBDA) (isomers that do not resolve in Mass spectrometry imaging (MSI) experiment).

Matrix-assisted laser desorption/ionization Imaging mass spectrometry (IMS, also termed mass spectrometry imaging (MSI)(MALDI-MSI) examines on the cross-sections of glucose leaves indicated that the cannabinoids did not originate in the leaf tissue itself, rather they came through the trichomes on the leaf's surface.

III. Chromatographic analysis

Brayan Jonas Mano-Sousa MS *et al.,* (2021) studied Color analysis technique as well as assessment of cannabis detection using thin-layer chromatography (TLC).The TLC techniques examined in this study have benefits over other analytical techniques because they are quick, easy, and effective in isolating and detecting cannabinoids. In this investigation, using FBBS or even FBRR in an acidic ethanol-based environment results in a colorimetric response for cannabis.

Si Huang, Ruiying Qiu *et al.,* (2022) reported Semiquantitative THC Analogue Screening using TLC Silica gel G with anRetention Zone Ag(I) along with Chromogenic Smartphone Detection. Whereas the Ag(I)-TLC smartphone approach suggested in this study provides for an accurate semiquantitative evaluation of total Tetrahydrocannabinolic acid, Tetrahydrocannabinol, and Cannabinol and may be used in the field as a quick screening tool over cannabis variety categorization.

N. Galand *et al.,* (2004) reported the Cannabis component separation and identification using several planar chromatography methods (TLC, AMD, Optimum performance laminar chromatography). Cannabis resins (0.1 grams) was extracted in this investigation by swirling at ambient temperature for 20 minutes with 10 mL of hexane. The mobile phase for the separation of 8-THC, 9-THC, CBN, as well as CBD was hexane and diethyl ether in the proportion of 80:20, v/v. THC, CBD, along with CBN were extracted by traditional way from cannabis resin and the Cannabis sativa plant.

As a result of AMD's excellent resolution and lack of spot stretching, it is possible to measure dose using scanning densitometry. By using OPLC in the semipreparative mode, CBN and 9-THC were separated from cannabinoids resin.

Justin T. Fischedick *et al.,* (2009) developed a Quantitative as well as Qualitative HPTLC Densitometry Method for Cannabinoids Analysis in Cannabis Sativa L. The plant material was extracted with ethanol and shaken for 15 min the whole extraction procedure was repeated twice. Chloroform was used as the mobile phase plus showed Rf values of 0.52 for Cannabidiol, 0.47 for Delta-9-tetrahydrocannabinol, 0.49 for Delta-8 tetrahydrocannabinol, 0.47 for Cannabinol, 0.47 for Tetrahydrocannabivarin, 0.47 for Cannabigerol, and 0.33 for cannabichromene. Separation of Cannabinoids is done by using C18 Waters Bondapakguard column. The mobile phase was a gradient of methanol and water with a 25 mM formic acid concentration; Methanol plus Water ratios ranged from 65: 35 to 100: 0 over 25 minutes, and isocratic to 28 minutes. The flow rate was 1.5 mL/min, with the total run time was thirty-two minutes. This method may also be used to screen the principal neutral cannabinoids found in cannabis variety.

UK Kulkarni *et al.,* (2018) developed the high-performance thin layer chromatographic technique for detecting cannabis in forensic interest, in which the cannabis standard was evaluated using HPTLC in multiple solvent systems. The three most important cannabis components for cannabis detection are THC, CBN, and CBD. Using a 9:1:1 solvent solution consisting of toluene, ethyl acetate and acetone, cannabinoids were separated using HPTLC.

Yifan Liu *et al.,* (2020) reported Cannabinoids data from ten mobile phase solutions for high-performance thin-layer chromatography (HPTLC),stationary phase used was 60 F 254 (2010cm) silica gel plates then mobile phase used was Hexane plus acetone in the proportion of 87:13, in volume by volume for cannabis biomarkers with detection wavelength: 254nm, where the supplemental material comprises the HPTLC reports (S2), RF data, and resolution data (S3, S4) of all ten systems' triplicate analyses.

Wieland Peschel *et al.,* (2015) reported In this work, that proton nuclear magnetic resonance (proton NMR, hydrogen-1 NMR) along with High-Performance Liquid Chromatography together with Diode-Array Detection were utilized for chemotype differentiation, extract profiling, as well specification of Cannabis sativa L. tetrahydrocannabinol (THC), cannabidiol (CBD), cannabigerol (CBG), their acidic counterparts (THCA, CBDA, CBGA),Cannabinol (CBN) and cannflavin A as well as B are quantified and used in two newly validated HPLC/DAD procedures for cannabis extract profiling along with identification using cannabinoids and other phenolics. To study the repercussion on the cell viability some tests were done (MTT test, Henrietta Lacks).

Virginia Brighenti et al (2017) developed a new extraction approach and HPLC method for the analysis of non-psychoactive cannabinoids in hemp. To analyze the target analytes in hemp extracts, a novel reversed-phase high-pressure liquid chromatography, technology was put forward and used in

conjunction with an ion trap mass analyzer, diode array (UV/DAD), and electrospray ionization-mass spectrometry (ESI-MS).

Sanja Zivovinovic, (2018) reported Cannabinoids within Cannabis sativa L. samples were determined using reversed-phase liquid chromatography and UV detection for recreational, medicinal, as well as forensic applications. The *Humuluslupulus L.* sample was extracted in an ultrasonic bath with ACN/H2O 1:1 for 15 minutes before being repeated three times. Eight cannabinoids were separated using a Kinetex XB-C18 HPLC column using 0.1% Formic Acid in Water as well as Acetonitrile with 0.1% Formic Acid (v/v) as solvent flow rates set to 0.8mL/min and temperatures 50 °C, appropriately. The detection wavelength of the detector was 220nm.

Ada C. Gallo-Molina *et al.,* (2019) reported THC extraction, separation, and purification from the hemp plant utilizing Supercritical fluid extraction (SCFE) plus solid-phase extraction (SPE). A sequential supercritical fluid extraction-Solid-phase extraction (SPE)method has been developed to extract tetrahydrocannabinol via high purity through Canna-bisSativa L plant matter. THC purity was determined by GC-FID to be 90.1%. To determine the concentration as well as purity of THC, 31 fractions were collected and evaluated using thin-layer chromatography (TLC) and RP-HPLC.

Mara Mandrioli *et al.,* (2019) developed RP-HPLC-UV Method for Rapid Identification of 10 Cannabinoids in Cannabis sativa L. In this case, the RP-HPLC-UV is employed for separation and detection.This study found that the 10 most significant cannabinoids may be quantitatively measured in 8 minutes with just single wavelength (220 nm). Even with the difficult elution sequence, an entire separation of the cannabigerolic acid, cannabinoid, Cannabidiol, and Delta also 9-Tetrahydrocannabivarin peaks (from 3.5 to 4.5 min) resulted.

Federica Pellati *et al.,* (2018) reported in this work, researchers developed new methods for analyzing bioactive substances in Cannabis sativa L. (hemp). The High-Performance Liquid Chromatography with diode array UV detector technique was employed to ascertain quantitative data on the psychologically inactive cannabinoids found in hemp inflorescences. HS-SPME's extraction of hemp's volatile components was examined by GC-FID.

IV. Hyphenated technique analysis

OierAizpurua-Olaizola *et al.,* (2014) reported Highly efficient liquid chromatography-mass spectrometry can be used to detect as well as quantify cannabinoids in hemp plant. To detect the primary cannabinoids found in extracts prepared from Cannabis sativa L. plants via supercritical fluid extraction, the HPLC-MS/MS approach was extensively improved and validated. Seven small cannabinoids were discovered using UPLC-qToF.

Lorenzo Calvi *et al.,* (2018) reported in this work that, the researchers employed HS-SPME in conjunction with GC-MS and LC-HRMS to evaluate the total quality of therapeutic inflorescence as well as macerated oils. A technique for analysis based on HS-SPME in hyphenation with GC-MS along with High-Resolution Mass-Spectrometry (LC-HRMS) was developed, validated, and used for detailed profiling along with fingerprinting of cannabinoids and

terpenes with two approved medicinal varieties of Cannabis sativa L. inflorescence and macerated oils.

Radmila Pavlovic *et al.,* (2019) reported Phytochemical study of two varieties of Cannabis sativa L. grown in the Italian Alps. Several analytical methods, including Headspace-solid phase microextraction, GC/MS, SDS-PAGE, LC-MS, GC-FID, and HPLC-high-resolution mass spectrometry, can accurately profile two types of altitude-cultivated plants.

Theresa Schmidt *et al.,* (2020) developed a method for identifying and quantifying cannabinol as biomarker for regional cannabis retting in an early sedimentary record using HPTLC-ESI-MS (electrospray ionization mass spectrometry). The detection and quantification of CBN, a cannabinoid that is an unambiguous molecular identity for the Hemp plant and then, as a result, a method of detection for ancient water returning of hemp in sediment samples, using HPTLC-ESI-MS.

Theresa Schmidt *et al.,* (2021) reported A rapid HPTLC-ESI-MS method for differentiating actual cannabinoids from inaccurate cannabinoids in diverse oils. This study used high-performance thin-layer chromatography in hypenation with electrospray ionization mass spectrometry to develop and validate an accurate, simple, dependable, and fast method for analyzing CBN, CBD, and 9-THC in commercially available CBD oils.

Janina K. Bowenetal, (2021) reported the effect of the extraction procedure on the chemical content of cannabis extracts from varieties of plants. 41 compounds were discovered and evaluated with a non-targeted profiling for gas chromatography-mass spectrometry , 15 phytocannabinoids were assessed using a qualitatively targeted assay for ultra-performance liquid chromatography-based tandem mass spectrometry (UPLC-MS/MS), and 24 elements were examined using inductively coupled plasma mass spectrometry.

Federica Pellati *et al.,* (2018) reported novel approaches for the characterization of bioactive chemicals in the hemp plant nonpsychoactive cannabinoids were profiled subjectively and quantitatively in this work utilizing an HPLC ESI-MS with MS2 detection. The cannabis volatile fraction's properties were found by modifying a unique HS-SPME-GC/MS detection method.

CONCLUSION

For thousands of years, both developing and developed nations have employed herbal remedies and their preparations to provide society and communities with primary healthcare. One of the most crucial and fundamental processes in the production of herbal preparations is quality control since the product's quality affects the security and effectiveness of medications. Quality control is mostly utilized for finished products as well as raw materials, excipients, and other ingredients.It is essential for trademark protection, avoiding defective goods, and improving consumer trust. It ensures that the company uses evidence-based research and data rather than subjective experiences to ensure that the services/products fit the standards.

Along with chemically synthesized medicine the quality control as well as standardization of herbal medications is important in their isolated form, extract, in any other herbal or polyherbal formulation which is greatly aided

by spectroscopic and chromatographic techniques. Cannabis sativa is a herbal medicinal plant with a variety of medical properties. The analysis of same is important for its use.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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