

Review

Active Pharmaceutical Ingredients in Medical Cannabis: Manufacturer Profiling, Standardization Challenges, and Technological Compatibility

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Abstract

The pharmaceutical development of cannabis-based medicinal products is challenged by significant variability in the quality, composition, and standardization of plant-derived active pharmaceutical ingredients (APIs). In Ukraine, despite recent legislative liberalization, a substantial shortage of standardized raw materials continues to limit the development of innovative dosage forms. This study analyses international practices among API manufacturers to identify technological parameters necessary to overcome domestic market barriers and support the implementation of advanced drug delivery systems. Content analysis was conducted on regulatory documentation, professional literature, and manufacturers' technical specifications. Candidate evaluation followed predefined inclusion and exclusion criteria. The study assessed compliance with Good Manufacturing Practice (GMP) requirements, extraction and purification technologies, the extent of analytical characterization, and batch-to-batch reproducibility. Purposive sampling enabled a comparative analysis of various technological approaches. Marked heterogeneity was observed in API standardization and analytical control indicators among manufacturers. Possession of a GMP certificate was found necessary but may be insufficient to ensure the pharmaceutical equivalence of materials. Differences in extraction methods and purification levels may affect stability profiles, pharmaceutical development strategies, and risk management related to final product quality. The findings demonstrate that manufacturer selection is a critical decision point in pharmaceutical development, with substantiated supplier choice directly influencing dosage form development and regulatory compliance.

Keywords: *Cannabis sativa* L.; standardization; pharmaceutical drug development; API producers; drug delivery systems; Ukraine



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1. Introduction

The medicinal use of *Cannabis sativa* (*C. sativa* L.) dates back to ancient traditional medicine systems worldwide and has served as a foundation for contemporary pharmacological interest [1].

Over the past decade, medicinal products derived from medical cannabis have been increasingly integrated into clinical practice worldwide. The evolving regulatory frameworks in the European Union, the United States, and Australia have significantly influenced the development of regulatory systems in other countries [2].

The growing number of countries permitting medical cannabis use in clinical settings necessitates the establishment of comprehensive systems for development and production, beginning with the cultivation of raw materials and the standardization of active ingredients [3]. In the context of global legislative liberalization, the pharmaceutical industry is transitioning from the use of substandard plant materials to highly standardized API that comply with GMP requirements [4,5].

C. sativa L. (commonly referred to as hemp) and its bioactive constituents, particularly cannabinoids, have been extensively investigated from both chemical and biological perspectives for several decades following the elucidation of the structure of its principal active compound, Δ^9 -tetrahydrocannabinol (Δ^9 -THC). The pharmacological and psychotropic effects of the plant are largely associated with this group of compounds, especially Δ^9 -THC, which is predominantly synthesized in the leaves and female inflorescences. In addition to Δ^9 -THC, cannabis contains a variety of non-psychoactive cannabinoids, including cannabidiol (CBD), cannabichromene (CBC), and cannabigerol (CBG), which exhibit diverse therapeutic properties. The plant also comprises numerous non-cannabinoid constituents representing different classes of natural compounds. Over 560 chemical constituents have been identified in *Cannabis sativa* L., including major and minor cannabinoids, terpenes, and other bioactive compounds relevant to pharmaceutical development and analytical standardization [6–9].

Extensive scientific research has examined the therapeutic potential of cannabinoids across multiple clinically relevant domains, such as chronic pain management, epilepsy, neurological disorders, and inflammatory diseases [10–14].

Amid the ongoing war in Ukraine, research has increasingly focused on the potential role of cannabinoids in managing post-traumatic stress disorder (PTSD), particularly among veterans and civilians experiencing prolonged combat-related stress [15–19].

Scientific research indicates that the chemical composition of *C. sativa* L. directs pharmaceutical development and informs the selection of delivery methods for active substances [20]. A number of articles are devoted to extraction methods [21–23], analytical techniques [24], and quality control [25]. The abundance of secondary metabolites, such as terpenes and minor cannabinoids, underscores the importance of extraction control to preserve the “entourage effect” and maintain compound stability [26–28]. The physicochemical profile of the raw material, whether as a pure isolate or a full-spectrum extract, affects the choice of excipients and the selection of quality control methods, both of which are essential to ensure batch-to-batch reproducibility of therapeutic effects [27]. Due to the low solubility of cannabinoids in water, nanoemulsions or self-microemulsifying drug delivery systems (SMEDDS) are often used to achieve stable gastrointestinal absorption [29–31].

Although APIs are widely available globally, standardization remains inconsistent. Differences in cultivation methods significantly affect the stability of secondary metabolite profiles. Such variability poses risks to the reproducibility of the physicochemical properties of final dosage forms [32].

These standardization challenges are evident in the State Pharmacopeia of Ukraine, which underscores the importance of physicochemical characterization and quality requirements for standardized cannabis extracts intended for pharmaceutical use [33].

In Ukraine, where legislation is being harmonized with EU standards, selecting an API supplier is a critical stage in pharmaceutical development.

Law of Ukraine No. 3528-IX, adopted on 21 December 2023, regulates the circulation of Cannabis plants for medical, industrial, and scientific purposes [34]. The law establishes a clear legal framework for the use of cannabis in scientific research, enabling legal studies within Ukrainian institutions. Consequently, the law facilitates large-scale clinical and laboratory studies of cannabinoids in Ukraine, which may serve as a foundation for new scientific advancements in medicine, pharmacy, and biology.

With the development of the cannabis-based pharmaceutical market in Ukraine and the implementation of pharmacy production technologies, it is increasingly important to analyse the API manufacturer landscape, assess manufacturer expertise, and compare product characteristics. A key motivation for this analysis is that, under the designation “standardized extract” of *C. sativa* L., global manufacturers supply substances with significantly different physicochemical properties. Consequently, selecting a specific API is a fundamental stage in pharmaceutical development rather than a routine procurement decision.

The current literature often bypasses the “technological docking” stage between the physicochemical profile of the raw material and its compatibility with innovative nanocarriers. These differences may influence manufacturing standards, authorization pathways, and quality assurance procedures, ultimately affecting the comparability and reproducibility of pharmaceutical products derived from *C. sativa* L.

This study aims to comprehensively map and technologically profile global Suppliers of medical cannabis APIs to assess their scientific value for pharmaceutical development in Ukraine. Instead of providing experimental validation of APIs, the research focuses on identifying technological patterns and variability relevant to pharmaceutical development.

This research presents the first structured technological mapping of the global medical cannabis API landscape in relation to Ukrainian pharmaceutical development. It constitutes an exploratory analysis of an emerging and under-researched field.

2. Search Strategy and Data Sources

A structured narrative review was conducted alongside a strategic landscape analysis. Unlike conventional literature reviews, this methodology integrates current regulatory data from manufacturers with pharmaceutical technology principles to provide a comprehensive framework for selecting APIs in emerging markets such as Ukraine.

2.1. Study Design and Information Sources

The methodological approach focused on a systematic collection of technological data and regulatory requirements rather than a quantitative statistical analysis of literature volumes. The methodology included content analysis of scientific literature, examination of the Ukrainian regulatory framework, and comparative evaluation of proposals from global manufacturers of cannabis raw materials and APIs for their potential application in pharmaceutical development.

The literature search was conducted using the following international scientometric databases: PubMed (5043 results), Scopus (4285 results), Web of Science (2850 results), and Google Scholar (123,000 results). The search encompassed publications from 2015 to 2026.

The search strategy utilized the following keywords and their combinations: *C. sativa* L., standardization, pharmaceutical drug development, API producers, drug delivery systems, and bioavailability of cannabinoids.

2.2. Study Selection Process

The selection process focused on identifying publications that provide specific technical data on cannabinoid extraction and stabilization. This data established the baseline for the subsequent evaluation of international API suppliers.

Articles meeting the inclusion criteria underwent full-text assessment to confirm eligibility for further analysis. The transition from the scientific literature search to the final selection of 24 suppliers followed a multi-stage evaluation process. Candidates were evaluated for compliance with the Ukrainian regulatory framework (Law No. 3528-IX) and international GMP standards. The selection was further refined using the following criteria: (1) technological features of the API, including extraction and purification methods; (2) quality and standardization levels; (3) recommended scope of application, particularly suitability for advanced delivery systems; and (4) applied research and development (R&D) capabilities.

2.3. Eligibility Criteria

The inclusion criteria were as follows: peer-reviewed scientific articles, including original studies and systematic reviews; official regulatory documents; pharmacopeia monographs and current technical documentation from manufacturers; and publications addressing technological, pharmaceutical, or regulatory aspects of cannabinoid-based medicinal product development.

The included studies addressed technologies for the extraction and purification of cannabinoids, the physicochemical standardization of cannabinoid APIs, and the development of drug delivery systems, including nanoemulsions, SMEDDS, and liposomes. Studies investigating the bioavailability of cannabinoids were also included. Publications in English and Ukrainian were considered.

2.4. Exclusion Criteria

The following sources were excluded from the analysis: articles from non-peer-reviewed sources; conference abstracts lacking complete methodological descriptions (except for market reports when no alternative data sources were available); publications focused exclusively on socio-cultural aspects or recreational cannabis use without pharmaceutical or technological relevance; outdated sources rendered irrelevant by significant regulatory or scientific developments; and publications with inaccessible full texts or broken links to official manufacturer resources.

2.5. Analysis of Scientific Literature and Pharmaceutical Development

Current approaches to the development of cannabinoid-based dosage forms were analyzed, with particular attention to challenges related to low bioavailability and chemical instability. The analysis focused on innovative delivery systems, including SMEDDS, nanoemulsions, liposomal forms, transdermal systems, and sublingual systems.

2.6. Regulatory and Legislative Analysis (Ukraine)

Legislative restrictions and opportunities in Ukraine were analyzed based on current regulatory legal acts as of early 2026. The analysis primarily focused on the Law of Ukraine No. 3528-IX, which determines the legal status of medical cannabis and the conditions of scientific activity [34]; Resolutions of the Cabinet of Ministers of Ukraine (No. 282 [35], No. 1123 [36], No. 589 [37]) regarding licensing, import quotas, and recategorization of cannabinoids; and Orders of the Ministry of Health of Ukraine (No. 812 [38], which regulates general rules for manufacturing and quality control, and No. 1586 [39]). The analysis also considered forms of medicinal products permitted for pharmacy production.

The list of permitted conditions is dynamic and is being expanded by the Ministry of Health (see Table 1).

Table 1. Prescribed Conditions and Permitted Dosage Forms in Ukraine.

List of Diseases and Conditions for Which Medicines Are Prescribed That Can Be Manufactured in a Pharmacy from the Plant Substance Cannabis	List of Dosages of Medicines That Are Entered into the Central Database of Medicines That Can Be Manufactured in a Pharmacy from the Plant Substance Cannabis
Chronic or neuropathic pain (R52.2) and/or spasticity (R25.2) caused by diseases such as: • malignant neoplasms (C00–C97); • diabetic neuropathy (E10.4, E11.4, E12.4, E13.4, E14.4); • multiple sclerosis (G35); • trigeminal neuralgia (G50); • facial nerve damage (G51); • neuralgia due to herpes zoster (G53.0); • nerve root and plexus damage (G54); • nerve root and plexus compression in diseases (G55); • mononeuropathies of the upper limb (G56); • mononeuropathies of the lower limb (G57); • polyneuropathies and other peripheral nervous system disorders (G60–G64); • cerebral palsy and other paralytic syndromes (G80–G83); • spinal cord injuries (S14.0, S14.1, S14.7, S24.0, S24.1, S24.7, S34.0, S34.1, S34.3, S34.7, T09.3, T91.3); • intracranial injuries (S06). Nausea and vomiting (R11) caused by chemotherapy (Z51.1) during the treatment of neoplasms (C00–C97). Parkinson’s disease (G20). Combined vocal tic with multiple motor tics (Tourette’s syndrome) (F95.2). Refractory (drug-resistant) epilepsy (G40–G41). Diseases causing seizures in childhood, such as Lennox–Gastaut syndrome (G40.4), Dravet syndrome (G40.4), tuberous sclerosis (Q85.1). Weight loss associated with anorexia (R63.0) in patients with diseases caused by human immunodeficiency virus (B20–B24). Other diseases (A00–T98).	Drug forms/Dosage of tetrahydrocannabinol (THC) • Liquid drugs for oral use—oral drops (oral solutions, emulsions, suspensions) 10, 15, 25 mg/mL • Hard capsules 2.5, 5, 10 mg • Oral paste 25 mg/g • Oral gel 10 mg/g Drug Forms/THC and Cannabidiol (CBD) Dosage • Liquid Drugs for Oral Use—Oral Drops (Oral Solutions) THC 10 mg/mL: CBD 10 mg/mL, THC 25 mg/mL: CBD 25 mg/mL
In parentheses after the names of diseases and conditions are the codes according to the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision.	The basis for prescribing cannabis medicinal products to patients with diseases defined in paragraph 8 of the List of Diseases and Conditions is the availability of relevant recommendations in industry standards in the field of healthcare or in scientific publications published in scientific journals indexed in the Web of Science Core Collection and/or Scopus databases and based on the results of clinical trials.

The requirements for mandatory registration of each transaction in the Electronic System for Accounting for Medical Cannabis Circulation and compliance with the Tetrahydrocannabinol (THC) content threshold (in dried straw of medical cannabis) of at least 0.3% for medical purposes were assessed.

2.7. Comparative Profiling of API Suppliers

For comparative analysis, 24 global suppliers of cannabis-based APIs were purposively selected. Selection criteria included frequent mention and high ranking in leading industry analytical reports, such as the Medical Cannabis Market Report 2024–2033 (IMARC Group), Global Medical Cannabis Market—Industry Trends and Forecast to 2032 (Data Bridge Market Research), and The Global Cannabis Report: 5th Edition (Prohibition Partners) [40]. These market reports were used solely for contextual industry mapping, not as primary

scientific evidence. The purposive sampling approach prioritized technological diversity over statistical representativeness. The study examines a diverse array of medical cannabis products that, although marketed as standardized, display considerable regulatory and technological heterogeneity in their API profiles and manufacturing origins. Manufacturer selection was informed by regulatory, geographical, and technological factors, with particular emphasis on European manufacturers due to the high degree of regulatory harmonization within the European Union, including adherence to GMP and pharmacopeia standards.

Manufacturers with registered APIs or documented regulatory interactions in Ukraine were also prioritized, as this indicates practical access to raw materials for domestic pharmaceutical development.

Data were collected from publicly accessible official manufacturer websites between 1 November and 31 December 2025. Limitations of the study: Only information available online during this predefined period was included in the analysis. No direct communication with manufacturers was conducted. Selection criteria included presence in international marketing reports and the level of R&D maturity. The comparison parameters included: technological features: extraction methods (CO₂ extraction, cold extraction), types of substances (isolates, distillates, full-spectrum oils); quality standards: compliance with European Union Good Manufacturing Practice (EU-GMP), Good Agricultural and Collection Practice (GACP) standards, availability of Drug Master File (DMF) and Certificate of Analysis (CoA); carrying out clinical research; possible specialization in R&D: suitability for the development of individual dosage forms. The GMP status of selected manufacturers was verified using official regulatory databases, including the EudraGMDP, FDA Orange Book, and publicly available records from Health Canada.

2.8. Synthesis and Systematization

To integrate the obtained data, a SWOT (Strengths, Weaknesses, Opportunities, Threats) analysis was conducted to identify strategies for selecting API suppliers for the Ukrainian market. Systematization of the results enabled classification of manufacturers by their ability to provide stable genetics and reproducible composition, which is critical for pharmaceutical development in line with the requirements of the State Pharmacopeia of Ukraine.

2.9. Terminology and Classification

Within this screening study, pharmaceutical terminology is applied according to the product's position in the manufacturing value chain, rather than as rigid, isolated categories. Given the emerging status of the Ukrainian market, the terms "botanical raw material", "standardized extract", and "API" are considered as points along a continuum. "API" may be defined specifically for materials where the manufacturer explicitly claims GMP compliance for pharmaceutical use. It is recognized that these categories may overlap in practice, and the analysis focuses on their functional transition into finished dosage forms.

To ensure regulatory consistency, this study adheres to the following quality standards: GACP for primary production; EU-GMP for API manufacturing; DMF as the primary documentation for active substance quality; and CoA for batch-specific quality verification.

3. Regulatory Framework in Ukraine

The legalization of medical cannabis in Ukraine represents one of the most significant and complex healthcare and pharmaceutical reforms in recent decades. The enactment of the Law of Ukraine No. 3528-IX on 21 December 2023 established the basis for a new high-tech industry integrating the agricultural sector, advanced chemical manufacturing,

and research-driven pharmaceutical production [34]. This legislative change marks a fundamental shift from total prohibition to stringent, lawful regulation, empowering R&D stakeholders to pursue innovation in the treatment of chronic pain, cancer, and neurological disorders.

Ukraine's current regulatory framework operates through a multi-tiered system of legal acts, with each successive level providing further detail to the provisions established by the preceding one.

Distinguishing between medical and industrial hemp is essential for scientific research. Legislation establishes a specific threshold for THC content: medical cannabis must contain at least 0.3% THC in the dried strain. This threshold is decisive for R&D activities in plant breeding. Research institutions developing new varieties are required to maintain genetic stability to prevent unintended reclassification from industrial to medical hemp, which would alter protection and licensing requirements. Additionally, THC has been added to the list of substances with restricted circulation, enabling research into its interactions with other cannabinoids, such as CBD, CBG, and cannabitol (CBN), within pharmaceutical development. The legislation also delineates research priorities by specifying diseases and conditions for which medical cannabis may be prescribed. The primary focus areas include palliative care, neurology, and oncology (chronic pain, chemotherapy-induced nausea); neurology (multiple sclerosis, epilepsy, Parkinson's disease); pediatric neurology (Dravet syndrome, Lennox–Gastaut syndrome); and infectious diseases (anorexia and weight loss associated with HIV / AIDS).

A significant restriction for developers is the prohibition of medical cannabis in smoking forms. This limitation encourages innovation in drug delivery systems, including the development of liposomal formulations, microemulsions, transdermal patches (pending future approval), and sublingual rapid-dissolution technologies. Special consideration is given to pediatric formulations, which must not exceed 25 mg/kg/day and require strict composition standardization [34,39].

Scientific institutions lacking in-house cultivation facilities must address the challenge of importing raw materials and seeds. This process is governed by a quota system, with allocations determined by the state based on applications from businesses and research organizations. Legislation permits the importation of seeds (at least second generation) and cannabis plant substances (API). However, exceeding the allocated quota, even for research purposes, is strictly forbidden. Consequently, R&D managers must accurately project material requirements one year in advance.

As a result, the regulatory constraints outlined above redirect attention from general raw material availability to the strategic selection of APIs, requiring a comprehensive analysis of the global suppliers' landscape.

4. Global Landscape of Cannabis APIs and Strategic Evaluation

A notable advancement is the authorization to manufacture medicines from medical cannabis in pharmacies. This provision facilitates the development of personalized medicine, allowing drug formulations to be tailored to individual patient needs based on physician prescriptions. For the scientific community, this enables research into the following areas:

- excipients and stability: investigation of how various excipients (such as oils, alcohols, surfactants) may influence the bioavailability of cannabinoids in pharmaceutical preparations;
- synergy of components: examination of the impact of terpenes, when added to primary formulations, on therapeutic outcomes;
- express control methodology: development of quality control protocols for pharmacy-compounded drugs to ensure precise THC and CBD dosing.

Scientific and technological standards for standardized medical cannabis extracts guided the selection criteria for API suppliers. Previous content analysis of systematic reviews, randomized controlled trials, and regulatory documents from the FDA, EMA, and WHO demonstrates that variability in raw materials and low bioavailability of THC and CBD require the use of GMP-certified extracts with validated analytical methods, such as high-performance liquid chromatography and gas chromatography mass spectrometry, as well as advanced delivery systems, including SMEDDS and nanoemulsions [41–49]. Consequently, manufacturer proposals were analysed to ensure reproducible pharmacological properties in future drug products. To support in-depth scientific analysis, suppliers of raw materials for standardized medical cannabis extracts were investigated to facilitate the development of new dosage forms (see Table 2). Most operate production facilities in multiple countries, and some function as integrated companies encompassing development, production, and distribution.

Variability in publicly disclosed data arises from differences in transparency and reporting standards among manufacturers.

Comparative analysis and systematization of collected information facilitate the identification of products offered by manufacturers of standardized cannabis raw materials.

Variations in medical cannabis raw materials among manufacturers are primarily linked to extraction technologies, purification levels, dosage-form orientation, and the degree of cannabinoid composition standardization. Analysis of these discrepancies enables classification according to the following characteristics.

4.1. Degree of Purification and Composition: Distinctions Between Isolates and Full-Spectrum Products

A comparative assessment of manufacturing approaches demonstrates a strategic divergence between botanical preservation and chemical isolation. Manufacturers vary in the degree of purification and the composition of final cannabinoid products. Some companies prioritize full-spectrum extracts, which retain a broader profile of cannabinoids and terpenes derived from the plant. Producers such as SOMAÍ Pharma and DEMECAN report extraction technologies designed to maintain a wide range of phytochemical constituents.

Other manufacturers focus on producing highly purified isolates or pharmaceutical-grade cannabinoids. For instance, Linnea SA and KD Phyto report the production of purified botanical isolates with high cannabinoid content for pharmaceutical applications.

A separate category comprises companies engaged in the development of registered cannabinoid-based medicines. Jazz Pharmaceuticals manufactures the cannabidiol-based medicinal product Epidyolex®/Epidiolex®, which has received regulatory approval from the FDA and EMA for specific indications.

4.2. Dosage Forms and Delivery Methods

Manufacturers differ in the dosage forms intended for cannabis-derived raw materials. Some companies supply standardized plant material, such as dried inflorescences used as a pharmaceutical raw material. Producers, including Bedrocan and Aurora Medical, describe such approaches.

Other manufacturers focus on raw materials designed for specific pharmaceutical formulations. For example, Panaxia reports the development of cannabinoid formulations for sublingual delivery systems and other specialized dosage forms. In contrast, KD Phyto describes the production of water-soluble cannabinoids and the use of nanoemulsion technologies to enhance formulation properties and bioavailability.

This results in a technological spectrum that ranges from traditional herbal forms, such as inflorescences, to advanced solubilization and nano-delivery systems.

Table 2. Comparative characteristics of manufacturers of standardized medical cannabis raw materials.

No.	Manufacturer (Country)/Website	Technological Features of API	Quality and Standardization	Recommended Scope of Application, R&D
1.	Aurora Medical (Aurora Cannabis) Edmonton, Alberta, Canada auroramedical.com	Supercritical CO ₂ extraction. Standardized forms include dried inflorescences, isolates, concentrates, oils, and topicals.	Declares products developed through scientific research that comply with Canadian regulatory requirements, EU-GMP certification.	Focuses on the development of smokeless delivery vehicles, such as topical dosage forms and capsules, and investigates the wellness effects of cannabinoids.
2.	Jazz Pharmaceuticals Palo Alto, CA, USA jazzpharma.com	Epidiolex (Cannabidiol)—cannabis-based medicine administered as an oral solution Epidyolex® in EU, UK, Australia and Israel. In the EU and U.K., Epidyolex is indicated for use as adjunctive therapy of seizures associated with LGS or DS, in conjunction with clobazam, for patients 2 years of age and older. In the United States, Epidiolex is indicated for the treatment of seizures associated with Lennox–Gastaut syndrome (LGS), Dravet syndrome (DS), or tuberous sclerosis complex (TSC) in patients 1 year of age and older. Epidyolex is also indicated for use as adjunctive therapy of seizures associated with TSC for patients 2 years of age and older.	FDA/EMA approval.	Orphan Drug.
3.	Bedrocan Veendam, Groningen, The Netherlands bedrocan.com	Standardized raw materials are produced to ensure consistent cannabinoid composition across batches.	EU-GMP certification; implementation of own GMCCP cultivation standards that exceed GACP requirements.	These materials may serve as reference samples for clinical research and the development of stable APIs.
4.	Tilray Nanaimo, British Columbia, Canada tilray.com	More than 50 strains were cultivated, and a cold extraction method was employed to preserve the cannabinoid and terpene profiles.	EU-GMP certification. The product is supplied with DMF, monographs, and comprehensive certificates of analysis.	Formulation and optimization of purified oral solutions and capsules for use in international clinical trials.

Table 2. Cont.

No.	Manufacturer (Country)/Website	Technological Features of API	Quality and Standardization	Recommended Scope of Application, R&D
5.	Tikun Olam Tel Aviv, Israel tikunolam.com	Full-spectrum (live-resin) oil, free from additives, is administered with precision dosing.	Information focuses on the 20 years of research and includes 17 peer-reviewed publications. GMP certification for pharmaceutical API production not confirmed in official regulatory databases.	Development of therapeutic formulations for gastroenterology, including a phase II study in Crohn's disease, as well as for pain and sleep disorders.
6.	Panaxia Lod, Israel panaxia.co.il	Reports conversion of plant-derived compounds into pharmaceutical formulations with enhanced bioavailability.	Production is conducted in compliance with IMC-GMP and EU-GMP requirements, incorporating rigorous process validation.	Formulation and evaluation of sublingual fast-disintegrating tablets, suppositories, and inhalable extracts administered via vaporizers.
7.	Linnea SA Riazzino, Ticino, Switzerland linnea.ch	Production of Highly Purified Botanical Isolates, Extracts, and Dilutions (>99.5% CBD/CBG).	40 years of experience operating under GMP standards, and comprehensive process validation ensures consistent composition stability.	The production of API is conducted for both parenteral and solid dosage forms.
8.	SOMAÍ Pharma Lisbon, Portugal somaipharma.eu	Production of full-spectrum oils through scientifically validated extraction techniques. Purification up to 97%. Removal of waxes and chlorophyll.	Attainment of EU-GMP certification and publication of peer-reviewed studies regarding oil production standards.	Advancements in soft gelatin capsules, oral sprays, and novel inhalation solutions.
9.	KD Phyto Homburg, Saarland, Switzerland kdphyto.com	Plant-based and synthetic cannabinoids, including water-soluble formulations.	Adherence to EU-GMP standards and International Council for Harmonization (ICH) guidelines.	Development of nanoemulsions, transdermal delivery systems, and customized nutraceutical formulations.

Table 2. Cont.

No.	Manufacturer (Country)/Website	Technological Features of API	Quality and Standardization	Recommended Scope of Application, R&D
10.	Linnaeus Health Madrid, Spain linneohealth.com	Expertise in industrial cannabis derivatives and pharmaceutical extracts.	EU-GMP Part I and II. Use of advanced analytical laboratory facilities to achieve compliance with global quality standards.	Contract manufacturing and the provision of raw materials to support the development of innovative pharmaceuticals.
11.	Medalchemy Alicante, Valencia, Spain medalchemy.com	The only manufacturer available in Ukraine. Full spectrum extract (the content THC 25 mg/mL; CBD 25 mg/mL; THC 10 mg/mL; CBD 10 mg/mL) (by the end of 2025).	GMP certification.	Products can be used in clinical trials or as APIs in drugs.
12.	MediPharm Labs Barrie, Ontario, Canada medipharmlabs.com	Purified concentrates (>80%) are produced in clean rooms that comply with ISO standards.	GMP certification is emphasized, with a particular focus on bioavailability studies of cannabinoid compounds.	The institution facilitates academic partnerships and supplies raw materials for clinical research.
13.	The Cronos Group Toronto, Ontario, Canada thecronosgroup.com	Scientific work aimed at unlocking the therapeutic potential of rare cannabinoids	Declares the creation of disruptive intellectual property is guided by rigorous standards of transparency and quality.	Advancement of novel technologies for the production of minor cannabinoids intended for targeted therapeutic applications.
14.	DEMECAN Dresden, Saxony, Germany demecan.de	Innovative product, Frischextrakt (fresh extract), which is produced using the Live Rosin method.	GMP certification.	The production of primary pharmaceutical formulations in pharmacies and the development of capsule forms utilizing proprietary extracts.
15.	Curaleaf International New York, NY, USA curaleaf.com	Vertically integrated production from cultivation to finished products reported.	EU-GMP certification reported.	Participation in clinical research collaborations.

Table 2. Cont.

No.	Manufacturer (Country)/Website	Technological Features of API	Quality and Standardization	Recommended Scope of Application, R&D
16.	Canopy Growth Smiths Falls, Ontario, Canada canopygrowth.com	Large-scale cannabis cultivation and processing.	Declares production is conducted on a global scale, with particular emphasis on the scientific investigation and disclosure of the plant's properties. GMP certification for pharma-ceutical API production not confirmed in official regulatory databases.	Research on medical and wellness cannabis products.
17.	Organigram Global Moncton, New Brunswick, Canada organigram.ca	Cannabis cultivation and extraction technologies reported.	Emphasize innovation in product development and systematic data collection regarding consumer properties; GMP certification for pharma-ceutical API production not confirmed in official regulatory databases.	Research on cannabinoid-based product development.
18.	Ilesol Pharma Varaždin, Croatia ilesol.com	Production of minor cannabinoids (CBG, CBN) and terpenes reported.	ISO/IEC 17025 [50] laboratory accreditation for analytical testing.	Development of combination drug therapies and customized formulations is available upon request. Analytical studies of cannabinoid composition and impurities.
19.	Essentia Pura Milan, Lombardy, Italy (pan-European production) essentiapura.com	Extraction technologies preserving plant components reported.	Each batch undergoes double testing, ensuring complete traceability from soil to oil; specific GMP certification for pharma-ceutical API production not confirmed in official regulatory databases.	Development and validation of customized CBD formulations for application in the pharmaceutical and nutraceutical industries.

Table 2. Cont.

No.	Manufacturer (Country)/Website	Technological Features of API	Quality and Standardization	Recommended Scope of Application, R&D
20.	Cansativa Group Frankfurt, Hesse, Germany cansativa-group.de	Distribution and logistics platform for cannabis products.	Supply chain quality control reported. Works with EU-GMP certified manufacturers.	Market access and distribution of APIs, supply of various APIs for pharmaceutical production.
21.	Celadon Pharmaceuticals Cambridge, England, UK celadonpharma.com	Full-spectrum oils production via indoor hydroponic cultivation and custom APIs designed for THC-dominant formulations.	EU-GMP registration with the MHRA, operates a proprietary track-and-trace system using individual QR codes and IoT modules for each plant, and holds a GPhC license.	Evaluation of Oral and Inhaled Formulations for Chronic Pain: Evidence from UK and EU Clinical Trials.
22.	Blossom Pharma Benavente, Santarém, The Netherlands blossompharma.com	Production of cannabis APIs and finished dosage forms.	EU-GMP Part I and II certification (simultaneously for API and finished dosage forms). Full validation of equipment for work with controlled substances.	Large-scale production of oils and isolates and their integration with pharmaceutical manufacturing.
23.	Extractions Solutions Villajoyosa, Alicante, Spain extractionsolutions.com	Specializes in the post-processing and refinement of <i>C. sativa</i> derivatives. Extraction technologies not specified.	Pharmaceutical laboratory authorization; GMP/NCF compliance certificate for active substances; GMP/NCF compliance certificate for medicinal products for human use; AEMPS authorization for manufacturers of narcotic active substances.	Standardized intermediates and customized APIs (CBD, THC).
24.	Cantourage GmbH Berlin, Germany cantourage.com	Production of CBD/THC API.	GMP/NCF compliance certificate for active substances.	Declare formulation as starting materials for pharmacies.

Notes: The table was compiled by the authors based on analysis of manufacturers' websites (Accessed December 2025).

4.3. Level of Standardization and Genetic Stability

The level of standardization of plant material is another distinguishing characteristic among manufacturers. For example, Bedrocan reports using genetically standardized cultivars to ensure consistent cannabinoid composition across production batches.

Other producers cultivate multiple cannabis varieties to achieve different cannabinoid profiles. According to publicly available information, Tilray maintains a portfolio of numerous cultivars for the development of differentiated cannabinoid compositions.

4.4. Therapeutic Positioning

Several companies report involvement in research on therapeutic applications of cannabinoids. For example, Jazz Pharmaceuticals focuses on developing cannabinoid-based medicinal products for neurological disorders. Other manufacturers describe research collaborations and clinical investigations addressing various therapeutic indications, including chronic pain, inflammatory diseases, and neurological conditions.

4.5. Extraction Technologies and Purity

Extraction methods constitute an additional differentiating factor among manufacturers. Reported technologies include supercritical CO₂ (SC-CO₂) extraction, cold extraction, and other purification methods designed to preserve cannabinoid profiles and remove impurities. The choice of extraction method distinguishes manufacturers targeting high-purity fractions from those prioritizing the “entourage effect”.

For example, Tilray reports using cold extraction methods to preserve volatile compounds, whereas other producers employ supercritical CO₂ extraction to obtain purified cannabinoid fractions.

Based on manufacturers’ reported technological characteristics, standardized cannabis raw materials may be used in various pharmaceutical research and development. These areas include the development of APIs with controlled cannabinoid composition, the investigation of novel delivery systems, and the study of cannabinoid pharmacology in clinical research settings.

Based on the analysis of the technologies of global manufacturers of medical APIs, several key technological directions can be identified in cannabis (Figure 1).

The results should be interpreted as identifying consistent technological patterns rather than as definitive comparative conclusions.

The selection of APIs in Ukraine involves a complex interplay of factors, requiring technological advantages to offset significant regulatory and safety risks, legislative constraints, and elevated raw material costs. A SWOT analysis was conducted to evaluate factors influencing the selection of raw material producers in the context of pharmaceutical development opportunities (Figure 2).

The SWOT analysis serves as a decision-support framework under conditions of regulatory uncertainty and limited data availability. Specific cases such as Medalchemy are referenced not for promotional purposes but as illustrative benchmarks for the technological standards essential to Ukraine’s integration of medical cannabis. This ‘supplier–developer’ model provides the most robust path for mitigating regulatory risks.

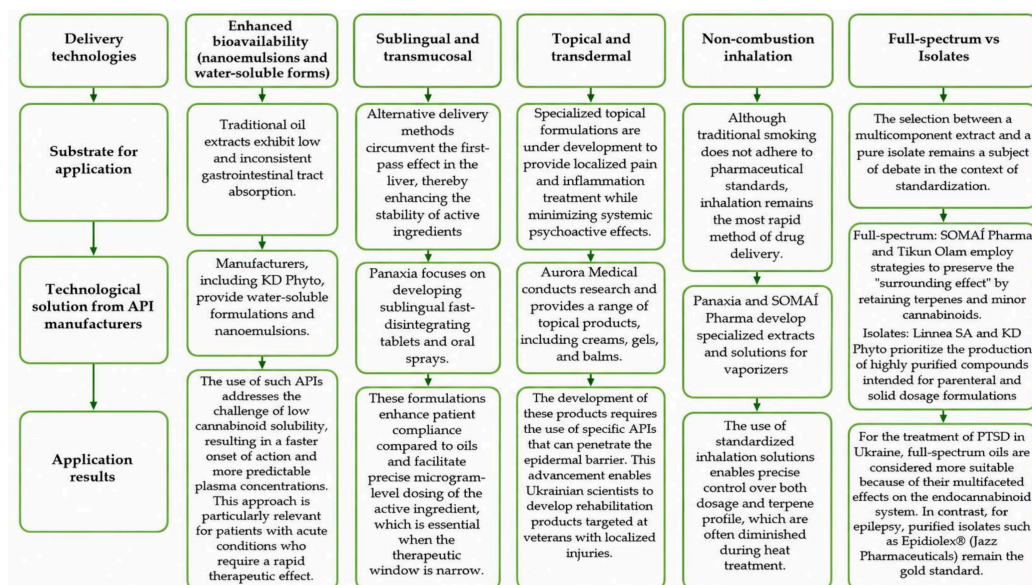


Figure 1. A Conceptual Framework for Selecting Medical Cannabis Delivery Systems: Integration of API Manufacturing Technologies and Pharmaceutical Formulations. Source: Compiled and synthesized by the authors.

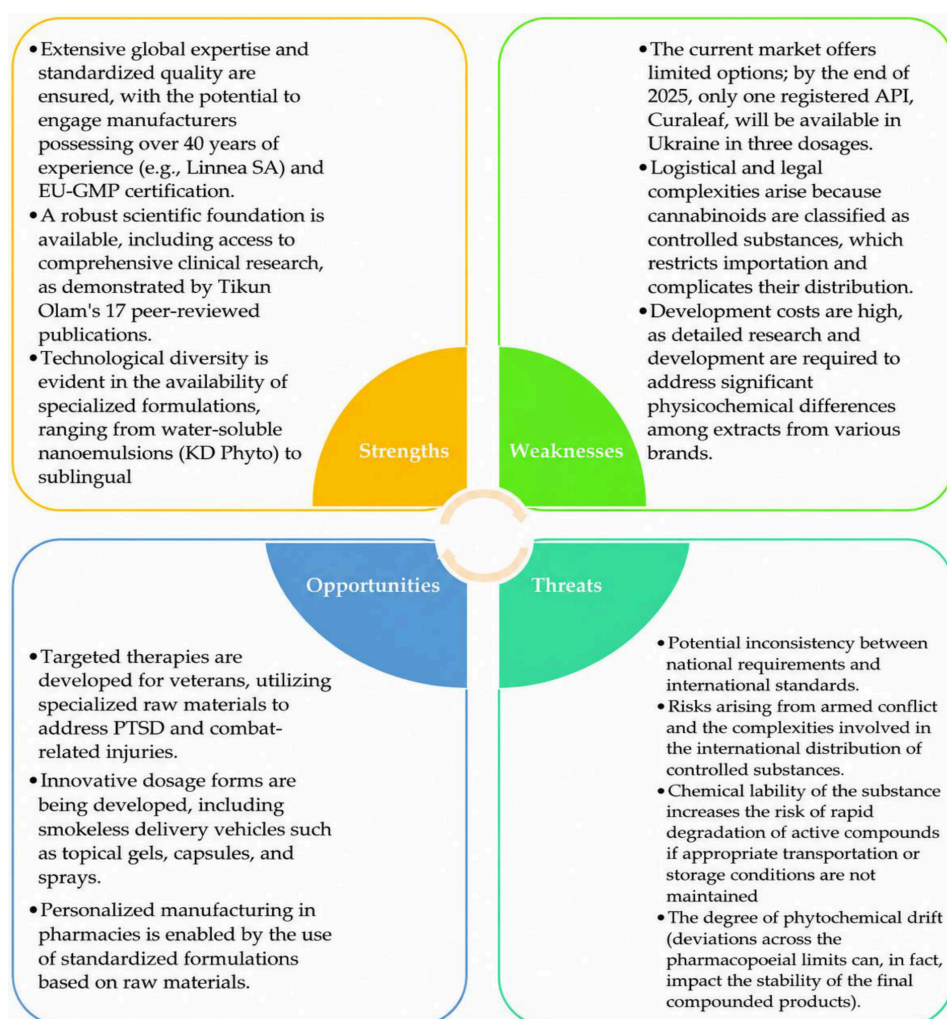


Figure 2. Strategic Evaluation of Medical Cannabis API Procurement in Ukraine: SWOT Analysis of Opportunities and Risks in an Emerging Regulatory Environment. Source: Compiled and synthesized by the authors.

5. Discussion

5.1. Technological Heterogeneity and Standardization Challenges

The findings of this study should be interpreted within the framework of an exploratory technological analysis aimed at identifying reproducible patterns rather than establishing quantitative correlations. The observed variability in data disclosure among global manufacturers highlights the absence of a unified international reporting standard for pharmaceutical-grade cannabis APIs. This inconsistency reflects not only differences in transparency but also heterogeneity in regulatory maturity and quality assurance practices across jurisdictions.

The transformation of botanical raw materials into pharmaceutical-grade APIs requires the application of intensified extraction technologies capable of ensuring chemical stability, selectivity, and reproducibility. Although conventional solvent extraction remains widely used, modern approaches such as ultrasound-assisted extraction (UAE) and SC-CO₂ extraction provide significant technological advantages. These methods enable selective fractionation of cannabinoids and terpenes through modulation of pressure and temperature parameters, thereby directly influencing impurity profiles, residual solvent levels, and physicochemical stability of the final API [20–22,28,48]. In particular, SC-CO₂ extraction preserves thermolabile compounds and reduces oxidative degradation, supporting a more stable and pharmaceutically acceptable product profile [22,23,51,52].

Analytical characterization represents a critical component of API standardization. While high-performance liquid chromatography (HPLC) remains the gold standard for cannabinoid quantification, emerging techniques such as quantitative nuclear magnetic resonance (qNMR) provide absolute quantification without reliance on reference standards. This is particularly important for minor cannabinoids, where certified standards are often unavailable. The use of qNMR reduces inter-laboratory variability and enhances reproducibility, which is essential for ensuring batch-to-batch consistency in pharmaceutical development [24,25,53].

The coexistence of highly standardized pharmaceutical APIs and variable manufacturer-defined extracts reflects a dual-track market structure. This phenomenon is consistent with findings from recent pharmaceutical studies, which indicate that compliance with pharmacopoeial specifications does not necessarily guarantee therapeutic equivalence due to variability in minor constituents and excipient interactions [27,33]. Such variability constitutes a critical risk factor in the development of reproducible dosage forms, particularly when dealing with complex botanical matrices.

5.2. Impact of API Characteristics on Advanced Dosage Forms

The pharmaceutical development of cannabinoid-based medicines requires not only standardized APIs but also a rational formulation strategy. The concept of “technological docking” introduced in this study refers to the alignment of critical material attributes (CMAs) of APIs with formulation parameters to ensure consistent drug performance. This concept is aligned with the QbD paradigm, where the physicochemical characteristics of the active substance directly determine formulation behavior and therapeutic outcomes [29,43].

For purified cannabinoid isolates such as CBD, formulation development typically relies on lipid-based delivery systems, including SEDDS and nanoemulsions. These systems have demonstrated significant improvements in oral bioavailability, with reported increases ranging from two- to five-fold due to enhanced solubilization and lymphatic transport mechanisms [30,31,48,49]. Such approaches are particularly relevant given the inherently low aqueous solubility of cannabinoids.

In contrast, the formulation of full-spectrum extracts presents a higher level of complexity due to the presence of multiple cannabinoids and terpenes, which vary depending

on plant chemotype. Terpenes play a dual role, influencing both pharmacological activity and physicochemical behavior. Experimental studies suggest that terpene composition may affect interfacial tension, emulsification efficiency, and drug release kinetics in lipid-based systems [26,28,54]. Consequently, variability in terpene profiles necessitates adaptive formulation strategies, including the selection of appropriate lipid matrices and surfactants.

Advanced delivery platforms, such as Pro NanoLipospheres (PNL), have been proposed to address this variability by incorporating natural absorption enhancers and stabilizing excipients. These systems enable improved bioavailability while maintaining formulation robustness despite fluctuations in API composition [41].

The physicochemical properties of cannabis-derived APIs, including purity, cannabinoid ratio, and terpene composition, directly influence solubility, interfacial behavior, and formulation stability. These parameters determine compatibility with delivery systems such as SMEDDS and nanoemulsions and ultimately affect the reproducibility of therapeutic outcomes.

Importantly, GMP certification alone does not fully ensure pharmaceutical equivalence. While GMP guarantees compliance with manufacturing processes, it does not eliminate variability inherent to botanical raw materials. Previous studies suggest that even GMP-compliant cannabis products may exhibit differences in cannabinoid composition and impurity profiles that could influence formulation performance and clinical consistency [25,30].

5.3. Implications for the Emerging Ukrainian Pharmaceutical Market

The development of the medical cannabis sector in Ukraine occurs within a highly regulated and resource-constrained environment. The limited availability of standardized APIs, combined with strict legislative controls, creates significant barriers to pharmaceutical innovation. Currently, the reliance on a restricted number of registered products limits the ability to develop diverse dosage forms, particularly solid and transdermal systems.

The variability in API characteristics identified in this study introduces additional complexity into supplier selection and risk assessment processes. For pharmaceutical developers in Ukraine, this variability necessitates a shift from traditional procurement strategies toward a more comprehensive evaluation framework that integrates technological, regulatory, and analytical criteria.

From a clinical perspective, the growing demand for cannabinoid-based therapies, particularly in the context of war-related conditions such as PTSD, underscores the importance of selecting APIs with well-characterized pharmacological profiles. The distinction between THC-dominant and balanced THC/CBD formulations is critical for therapeutic efficacy and safety. Scientific evidence supports the need for precise standardization to ensure predictable pharmacodynamic effects across patient populations [15–17].

The authorization of pharmacy-based compounding represents a significant opportunity for personalized medicine in Ukraine. However, the successful implementation of this model depends on the availability of APIs with consistent quality attributes. International models, such as the distribution framework employed by German companies, demonstrate the feasibility of integrating standardized APIs into pharmacy practice, providing a potential roadmap for the Ukrainian market.

5.4. Methodological Contribution: The Comparative Mapping Tool

A key contribution of this study is the identification of a critical gap between formal standardization and functional reproducibility of cannabis-derived APIs. The proposed comparative mapping approach provides a structured framework for evaluating manufacturers based on technological, regulatory, and analytical parameters.

This approach enables researchers and pharmaceutical developers to move beyond descriptive market analysis toward a more systematic assessment of API suitability for drug development. By integrating data on extraction technologies, analytical characterization, and formulation compatibility, the framework facilitates the alignment of cannabis-derived APIs with established pharmaceutical quality systems.

Importantly, the findings suggest that the primary limitation in the current market is not the availability of cannabinoids per se, but rather the lack of consistent technological transparency and standardized reporting practices among manufacturers.

5.5. Limitations and Future Directions

Although this study provides valuable insights, its scope is confined to an initial market screening. The analysis primarily describes the product landscape in Ukraine under the new regulatory framework, based on available data and technical specifications. A significant limitation is the exclusive reliance on manufacturer-declared information. While this approach is appropriate for preliminary market assessment, it is important to distinguish between regulatory-validated documentation (such as EU-GMP certifications or DMF summaries) and marketing-driven claims presented on corporate websites. This reliance on self-reported data introduces potential bias, as manufacturers may emphasize specific technological strengths while omitting detailed analytical or stability data. Consequently, the findings reflect the declared technological capabilities and strategic positioning of producers, rather than independently verified experimental outcomes.

Future research should include more detailed technological profiling through direct engagement with manufacturers to obtain comprehensive CoA. Subsequent studies should progress from theoretical technological coupling to experimental validation of API compatibility with innovative delivery systems, such as SMEDDS. This approach will facilitate the development of practical manufacturing protocols for standardized cannabis-based medicinal products.

6. Conclusions

The study provides a comprehensive analysis of the technological and regulatory landscape for medical cannabis APIs, leading to the following conclusions:

- (1) Successful pharmaceutical development in Ukraine depends on selecting manufacturers that integrate R&D with validated analytical methodologies. Such integrated approaches ensure that APIs are compatible with advanced delivery systems, including controlled-release and non-inhalation routes.
- (2) Regulatory frameworks are not merely legal constraints but active drivers of formulation strategy. Integrating regulatory analysis at the early stages of R&D is essential to mitigate risks and ensure that dosage forms meet international standards (EU-GMP, GACP).
- (3) The selection of cannabis-derived APIs is a multidimensional process. Formal pharmacopoeia compliance is a baseline, but functional reproducibility depends on manufacturer-specific technological transparency and batch-to-batch consistency.
- (4) The proposed framework enables Ukrainian researchers and pharmacies to move from price-based procurement toward the Quality by Design principle. This approach ensures the predictability of therapeutic effects, even when utilizing heterogeneous starting materials.
- (5) While exploratory in nature, this study serves as a conceptual roadmap for the emerging Ukrainian market, particularly for the development of individualized THC/CBD formulations in pharmacy settings under the new legislative framework (Law No. 3528-IX).

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