

The potency puzzle

Understanding cannabis in the modern age

Traditional methods of chemical testing cannabis potency often fall short in accurately capturing the complex interactions between cannabinoids and the human body. This leads to challenges in identifying relevant medicinal cannabinoids, ensuring consistency in product potency and consumer confidence. However, the innovative CannaMetrix EC50 Array™ technology offers a solution. By measuring cellular responses to cannabinoids in real-time, this high-throughput method provides valuable insights into a product's true potency and therapeutic benefits, enhancing efficiency and reliability in the cannabis industry.

The cannabis and hemp industry's primary focus revolves around the measurement and regulation of products. This is based predominantly on the percent composition of delta-9-tetrahydrocannabinol (THC) – a cannabinoid typically found in *Cannabis sativa* and psychoactive agent – indicative of the ever-evolving nature of both the medicinal and adult-use markets. With the introduction of boutique cannabis products into these markets, there has been a noticeable surge in the diversity of cannabinoid content available to consumers, marking a pivotal moment in the industry's trajectory.

CannaMetrix, LLC has secured a patent for its groundbreaking technology, enabling the accurate demonstration of cannabinoids' genuine potency on

the human endocannabinoid system (a naturally occurring physiology in human cells that reacts to plant cannabinoids). This innovative approach empowers the formulation of products with precisely determined, dose-dependent effects on specific cell surface cannabinoid receptors. As a result, C Owen Wolffsmith and Harold C Smith's research from CannaMetrix, LLC helps consumers make better choices, improves satisfaction, and builds strong loyalty to the product.

CANNABINOIDS AND THE HUMAN PHYSIOLOGY

The standard cannabinoid panel typically consists of various compounds found in cannabis, including CBD (cannabidiol), Δ9-THC (delta-9-tetrahydrocannabinol), Δ8-THC (delta-8-tetrahydrocannabinol), CBG

(cannabigerol), CBC (cannabichromene), CBN (cannabinol), CBDV (cannabidivarin), THCV (tetrahydrocannabivarin), CBDA (cannabidiolic acid), CBGA (cannabigerolic acid), and THCA (tetrahydrocannabinolic acid).

These are all different cannabinoids found in cannabis, each with unique chemical structures and potential effects on the human body. However, measuring the amount of several cannabinoids in a product (current compliancy testing) may not fully capture the complex interplay between cannabinoids, their interactions with cell receptors, and consequential effects on human physiology. As a result, consumers face challenges in accurately gauging the potency and therapeutic efficacy of cannabis products.

While the physiological effects of THC (the primary psychoactive compound in cannabis, responsible for inducing the euphoric 'high' commonly associated with marijuana use) and CBD (a non-psychoactive cannabinoid found in cannabis known for its diverse therapeutic properties including anti-anxiety, anti-inflammatory, neuroprotective, and anticonvulsant effects) are widely recognised, scientific literature suggests that numerous minor cannabinoids can also play crucial roles in altering human physiology.

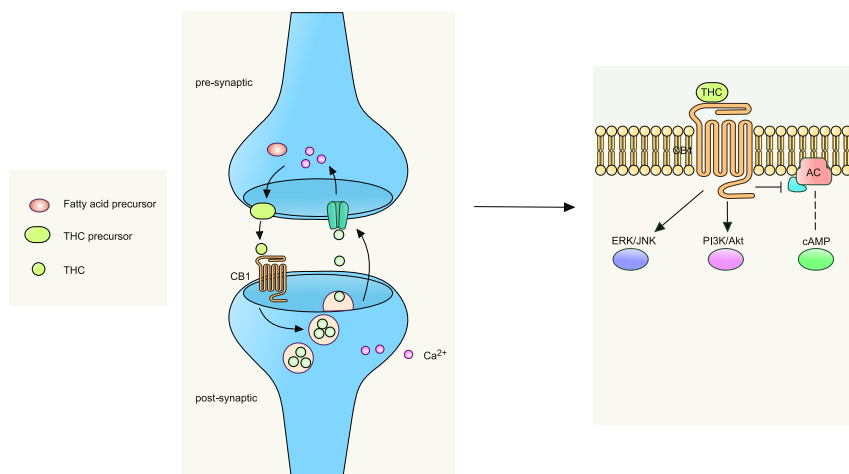
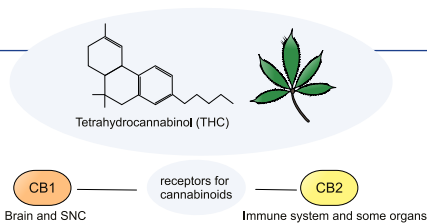
Moreover, the major and minor cannabinoids as well as terpenes acting in concert on the human endocannabinoid system can lead to responses distinct from those observed with individual cannabinoids, underscoring the complexity of cannabis' effects on the human body.

UNDERSTANDING THE LUKEWARM INDUSTRY RESPONSE

Despite this growing body of knowledge, the industry's approach to potency



By using human-origin cells engineered in the laboratory, the EC50 Array™ swiftly measures cellular responses to cannabinoids in real-time.



Cannabinoids are compounds found in cannabis that interact with proteins on the surface of cells (receptors) that serve as sensors and transducers of information into the interior of the cells to modify their biochemistry. Cannabinoid receptors, therefore, are the first to sense what cannabinoids are present and communicate this information to the endocannabinoid system – a network in the human body involved in regulating various physiological processes.

When cannabinoids bind to these receptors, they can trigger activation or inhibition of cellular functions. The 'entourage effect' refers to the phenomenon that results from multiple cannabinoids and other compounds that cannabis produces, acting concertedly on different receptors in different cells throughout the human body. The entourage effect is a more significant effect than the sum of the effects of the individual chemicals.

Each cannabinoid has its own potency and effectiveness, with some cannabinoids capable of very high levels of potency at low concentrations. When these minor composition cannabinoids are combined with other cannabinoids in specific blends, the collective potency experienced by a consumer can vary significantly from that inferred from their individual percent composition. This underscores the significance of evaluating how human cells respond to the particular composition in a cannabis product as the basis for assessing a product's potency. The primary concern in basing potency only on chemical composition is that cannabinoids overlooked as minor due to their low percent composition in a product, can have major impacts on how other cannabinoids impact the endocannabinoid system and therefore, the biologic potency perceived by a consumer.

determination remains somewhat rudimentary. Instead of embracing novel or targeted methods of assessing potency, producers often rely on consumer trends to inform product formulation, a reactive approach that may not fully capture the nuances of product potency.

Furthermore, studies conducted by reputable institutions, such as the FDA, NIH, JAMA, and Johns Hopkins, have shed light on discrepancies between labelled and actual cannabinoid content in products, further complicating consumer choice and highlighting the need for more robust quality control measures.

Understanding the historical context of cannabis regulation is crucial for comprehending the current state of the industry. THC's classification as an

However, as cannabis and cannabis research have gained mainstream acceptance, it has become increasingly evident that the interplay between major and minor cannabinoids is far more intricate than previously assumed, necessitating a paradigm shift in how potency is assessed and understood.

WHY SHOULD WE ASSESS THE BIOLOGIC POTENCY?

Distinguishing between chemical composition and biologic potency is paramount in accurately assessing the efficacy of cannabis products. While the percentage of THC by weight in a product is often colloquially referred to as its potency, this measure is somewhat arbitrary and does not necessarily correlate with therapeutic efficacy.

Biologic potency, on the other hand, considers both the dose of a

The interactions between major and minor cannabinoids as well as terpenes with the human endocannabinoid system can lead to responses distinct from those observed with individual cannabinoids.

illicit substance has historically hindered scientific understanding and discouraged research into the endocannabinoid system, perpetuating misconceptions and impeding progress in the field.

compound and the intensity of the body's response, offering a more nuanced understanding of a product's potency and its effects on the endocannabinoid system.

CANNAMETRIX EC50 ARRAY™ – PIONEERING A PARADIGM SHIFT

Innovative methods, like the CannaMetrix EC50 Array™, are closing the gap between chemical composition and biological potency in cannabis products. Developed by CannaMetrix, a leading expert in cannabinoid potency assessment, this technology provides a streamlined approach to gauging the biological impact of cannabis.



Cannabinoids interact with proteins on the surface of cells (receptors) that serve as sensors and transducers of information into the interior of the cells to modify their biochemistry.

By offering a deeper understanding of how cannabis interacts with the body, the EC50 Array™ empowers producers to refine plant genetics, extraction conditions, and product formulations, ensuring consistency and enhancing consumer trust.

By using human-origin cells engineered in the laboratory to produce a quantifiable and dose-dependent response to cannabinoids, the EC50 Array™ swiftly measures cellular responses to cannabinoids in real-time. This process evaluates the concentration of cannabinoids required to trigger a half-maximal response (EC50), offering valuable insights into a product's true potency and potential therapeutic benefits and enabling an understanding that pairs chemical composition with biologic potency.

In essence, it helps determine the effectiveness of the product in eliciting a desired response from the cells, which can then be correlated with its potential effects on the human body. By offering a deeper understanding of how cannabis interacts with the body, the EC50 Array™ empowers producers to refine plant genetics, extraction conditions, and product formulations, ensuring consistency and enhancing consumer trust. While chemical analysis remains vital for quality control, independent biological potency testing is pivotal

in guaranteeing the effectiveness and reliability of cannabis products.

COMBINING CHEMICAL AND BIOLOGIC POTENCY TESTING – A SAFE WAY FORWARD

By embracing more sophisticated methods of potency determination, producers can better meet the needs of consumers and provide products that deliver predictable and quantifiable effects, ultimately advancing the cannabis industry and enhancing public health and safety.

The cannabis industry is undergoing broadscale expansion with its evolving legal status. Consequently, a critical mass of technology to produce plant extracts and synthetic cannabinoids has flooded the market space with new products. Largely backed by industry status quo using anecdotal accounts of product performance, no direct testing or validation of biological potency for new products is introduced to consumers. With the pending US federal reclassification of cannabis to schedule III (controlled drug), producers

will need to adhere to higher standards associated with FDA oversight.

Current regulatory practices focus on quantifying specific cannabinoid content by mass percent. This principally establishes a threshold for THC-mediated intoxication; however, the same metrics are also erroneously being applied to cannabinoids of every type.

The researchers emphasise that predicting the interaction between plant cannabinoids and the human endocannabinoid system, crucial for the qualitative experience, goes beyond mere percent cannabinoid composition. A true measure of how combinations of cannabinoids of varying percent composition will trigger the endocannabinoid system can only be quantified through human biologic endpoints. Chemical testing alone fails to provide sufficient insight into a product's performance, especially for those marketed for effects other than THC's psychoactivity.

Biologic potency testing, measuring outcomes at the cellular level, becomes essential. Analogously, cannabinoid products resemble jars of assorted jellybeans, where legal limits dictate bean colours per jar. While colour represents chemical testing, flavour, reflecting combinations of colours, is assessed through biologic testing.

ADVANCING THE CANNABIS INDUSTRY

CannaMetrix, LLC's assay unveils unexpected potencies in cannabinoid blends, transcending individual cannabinoid tests or chemical composition analyses. The adoption of biologic potency testing will provide the cannabis industry with a means of evaluating plant growth, plant extracts, and synthetic blends before bringing products to market.

CannaMetrix, LLC has patented its technology and can demonstrate the true potency of cannabinoids on the human endocannabinoid system. This technology will allow for the formulation of products with known dose-dependent outcomes, on specific cell surface receptors, and result in informed consumer choice, satisfaction, and product loyalty.

Behind the Research



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Research Objectives

Researchers at CannaMatrix, LLC introduce the EC50 Array™ which unveils potencies in cannabinoid blends, transcending individual cannabinoid tests and chemical composition analyses.

Detail

Bio

Charles Owen Wolffsmith, PhD, is the Chief Scientific Officer of CannaMatrix with over 10 years of experience in biochemistry, bioenergetics, signal transduction, and metabolomics.

Harold C Smith, PhD, is the Founder & CEO of CannaMatrix, Oyagen, and Professor Emeritus at the University of Rochester. Smith has over 45 years of research experience in RNA biology, and over 20 years of experience in biotech and drug discovery.

Competing interest statement

The authors have financial interests in CannaMatrix, LLC and its patented method for testing the biologic potency of cannabis products based on the endocannabinoid system in human cells (US 11,782,050 B2). The Company seeks to transform the legal cannabis industry by differentiating products that have proven their potency to bring about dose-dependent responses from the human endocannabinoid system. In the researchers' opinion, the industry's reliance on percent of individual cannabinoids in a product as the sole metric to infer potency is misleading because combinations of major and minor cannabinoids bring about a combination or entourage effect in a living human cell that can be drastically different from the effect that chemical composition anticipates.

References

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Personal Response

Can you discuss any notable findings or trends observed in biologic potency testing using the EC50 Array™ across different types of cannabis products and formulations?

Our preliminary findings can be summarised in three points: 1) Most cannabinoids have a measurable activity on human cannabinoid receptors; 2) Isolating specific cannabinoids to 99%+ purity often results in decreased performance of the isolate relative to the blend or extract it originated from; and 3) Prepared mixes of pure cannabinoids in the exact mass percentages measured by chemical testing do not reproduce the same activity seen when measuring the broad or full spectrum products.

Therefore, we conclude that the cell-based potency testing provides an unbiased means of quantifying the combined potency of all cannabinoids simultaneously on their endocannabinoid target.

