Shining light on the growth path of a new industry – Measurement technology for medicinal cannabis production

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Across the globe, legislation surrounding the application of cannabinoid compounds towards human health is gaining momentum. Corresponding with new regulations is a dramatic increase in cannabinoid-based treatment options – from just a few drugs in the early 2000s to now over 300 cannabinoid-based treatment options currently in human trials for ailments such as post-traumatic stress disorder, nervous system degeneration, depression, epileptic seizures, Parkinson's disease, multiple sclerosis and schizophrenia. In 2017 alone, global cannabis-related companies raised over $2.0 billion USD, with cannabinoid-based pharmaceuticals market size in the U.S. expected to grow from $2B USD in 2020 to $20B by 2025 and $50B by 2029 [1].

The *Cannabis sativa* plant includes a variety of compounds such as cannabinoids, terpenes and phenolic compounds [2]. Cannabinoids and terpenes largely concentrate on the secretory cavity of the grandular trichomes of female flowers (see Figure 1 for the main plant components). There are over 100 different cannabinoid compounds that have been identified within the *Cannabis sativa* plant, and the concentration of these compounds depends on tissue type, age, variety, growth conditions (nutrition, humidity, light level), harvest time and storage conditions [3]. In other words, while the female flower trichomes are of greatest production interest, the leaves and stems may also be harvested based on the specific chemical compound of pharmaceutical interest. Figure 1 shows the three main plant components of a *Cannabis sativa* plant that are of interest.

Figure 1: The *Cannabis sativa* plant (*Source: Rua Bioscience*)

Cannabinoids begin as cannabidiolic acid or CBDA, and undergo a decarboxylation process to transform its chemical structure into other compounds such as THCA (*Delta-9-Tetrahydrocannabinolic Acid*). An example of the decarboxylation is when raw cannabis flowers containing THCA (which is non-psychoactive) is heated during recreational smoking. The heat will decarboxylase the THCA into THC (*Tetrahydrocannabinol*), which is a psychoactive compound.

The most well-recognised cannabinoid compound is probably THC, which has psychoactive compounds that contribute to its popularity in recreational use. However, the compound believed to have the most medicinal benefits is cannabidiol or CBD, which is a non-psychoactive compound. In general, medicinal cannabis growers would normally select strains that are CBD-dominant while recreational cannabis growers would prefer strains that are THC-dominant. Upon harvest, the cannabis products are chemically analysed in licensed laboratories to profile their chemical compounds, which then determines the concentration of the cannabinoid-of-interest and therefore sets the value of the crop.

Unfortunately, the chemical testing performed at the harvest stage of production is essentially aimed solely at meeting the quality standards for the pharmaceutical industry while providing little support for the producer or grower. This is because at this stage, the test results come too late to alter any decisions that led to the production of the crop. Thus, the industry needs reliable cannabinoid tests not only in dedicated quality control or certification labs, but also within the cannabis production cycle in order to support cultivation management, optimise yields and improve the quality and consistency of their produce. This requires rapid testing capability in or close to the cultivation facility. Figure 2 provides an overview of the possible testing needs during the production cycle.

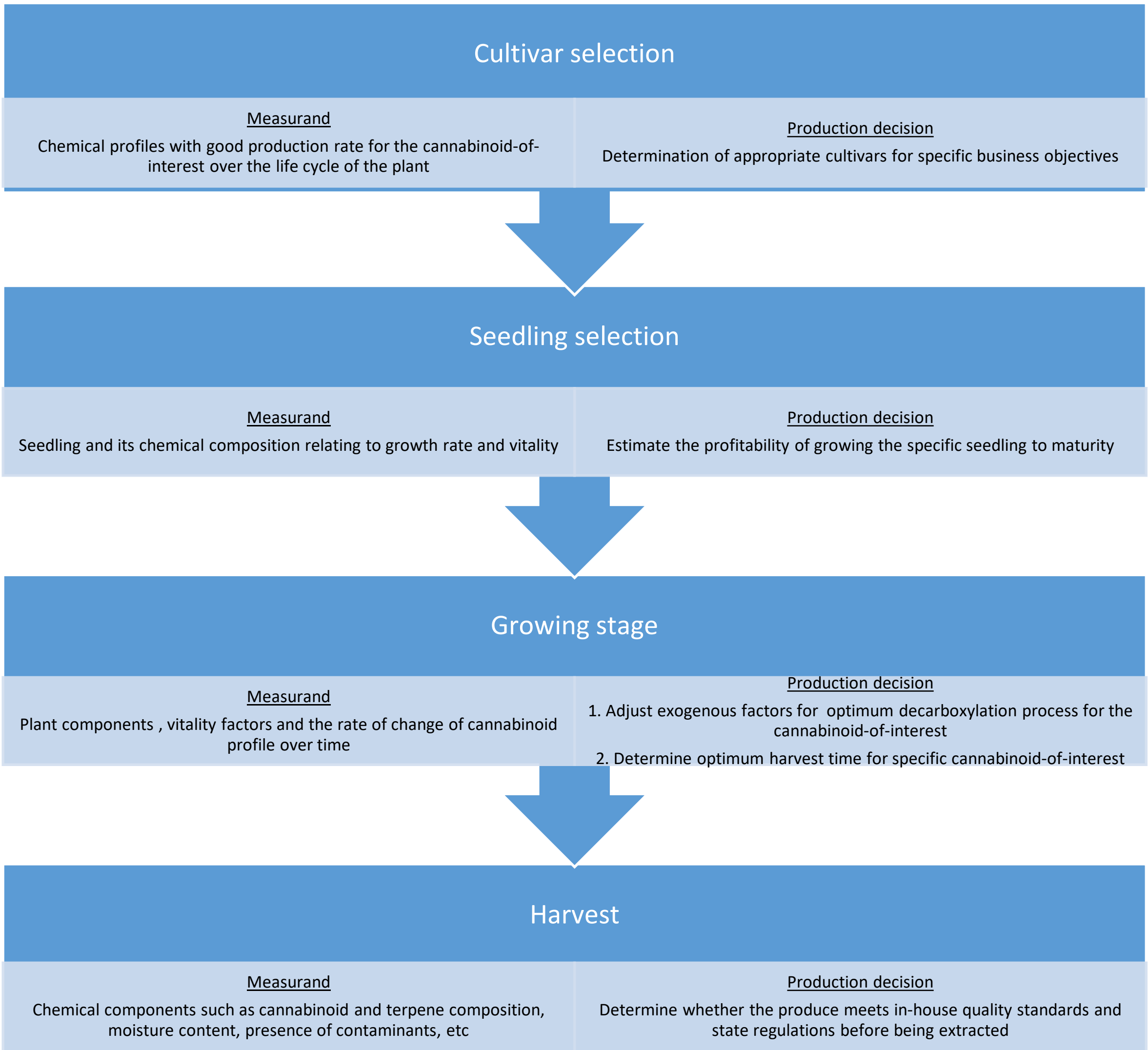

Figure 2: Overview of testing needs in cannabis production

Successful medicinal cannabis production relies on the selection of the best cultivars to produce plant material for a specific pharmaceutical product. Cannabis producers will select and purchase cultivars from companies that have breeding programmes to produce cultivars with specific chemical profiles. The selection criteria is based on the cannabinoid-of-interest i.e. a different cultivar will produce a different specific cannabinoid profiles. Successful breeding programs require detailed testing of the growing plants frequently without disturbing the plants themselves. Removal of physical samples is limited as only so much of a plant can be sampled before it is significantly affected. Therefore, optical measurement technologies have a clear advantage here as they can measure very frequently without influencing the growing plants that are to be assessed.

Testing during seedling selection (approximately 1-4 weeks upon planting) may be the first step towards estimating the profitability of the specific seedling for a specific business objective. At this stage, the early-stage growth rate can be used as a predictive model on the harvest potential of the plant and seedlings growing unsatisfactorily can be eliminated.

Test and monitoring during the growing phase is probably of greatest interest to cannabis producers. Since cannabinoid compounds are a result of a decarboxylation process, the concentration of specific cannabinoid compounds will differ depending on the stage of plant growth. Furthermore, all exogenous treatments to the plant such as trimming, fertilisation, watering, variations in light exposure cycle and temperature variations must be optimised and kept consistent to ensure that the cannabis crop is able to produce consistent quality and concentration of the specific cannabinoid-of-interest. Since the type and concentration of cannabinoids (in addition to potential impurities) can vary greatly from plant to plant (even of the same cultivar), this puts significant costs on the grower and producer to qualify and assess the product.

Some significant testing challenges during production were identified in [1], specifically: (1) lack standardised testing and (2) reducing the risk of “touching the plant”, especially when testing during the seedling selection and growing phases. Removing plant material for sampling can have considerable effects on a plants biochemistry and the sampled plants may develop differently from unsampled plants, thus introducing a systematic error into the testing regime. Furthermore, plant samples are controlled substances themselves and require an appropriate documentation process to ensure accountability for all removed plant material. Thus, “not touching the plant” is greatly preferable within the regulations and regional laws for cannabis cultivation in many jurisdictions.

It appears that an ideal measurement system for use in a cultivation environment should be able to test for cannabinoid concentrations at a reasonable precision (for a production environment in contrast to a certification laboratory) and:

- Be able to test plants without requiring the removal of plant material
- Be able to test many plants quickly
- No cost in consumables per tested plant
- Low labour cost, test either fast or automated
- Low equipment cost

These requirements are driving the global cannabinoid testing market, which is expected to reach $1.4 billion by 2021. With the amount of investment and interest in the cannabinoid-based pharmaceutical options, the further challenges of managing variation between plants, and managing variations of the same plant under differing growing conditions, it is clear that a significant focus of investments has been towards new instrumentation and measurement technologies that support the medicinal cannabis production.

Table 1 shows a non-exhaustive list of test technology either have been recently introduced, or are currently under development to support the cannabis production process. Each of their potential advantages and disadvantages are also listed for easy comparison. For "non-touching" monitoring and test, optical systems appears to have good promise for future development. However, these technologies still have many challenges to overcome in terms of equipment cost and test precision before they can become acceptable mainstream test methodologies.

Table 1: Examples of instrumentation and test equipment for medicinal cannabis cultivation

Technology	Advantages	Disadvantages	Examples
Laboratory Benchtop System for laboratory near cultivation area	- Set up in controlled environment - Highest precision standards possible	- Requires taking of physical samples - Labour intensive - Expensive equipment and sometimes consumables - Time delay for samples to be taken to lab	GemmaCert https://gemmacert.com/ Allied Scientific Luminary Beacon https://alliedscientificpro.com /shop/product/cannabis-thc-cbd-smart-analyzer-luminarytm-beacon-21342
Fieldportable Lab System	- Field mobile - Can reach high precision	- Requires taking of physical sample - Very labour intensive - Expensive device and consumables	Orange Photonics LightLab (https://www.orangephotonics.com/) Icon Scientific Anser Analyzer https://www.iconsci.com/product/ the-anser-cannabis-hemp-analyzer/
Handheld device for optical measurments	- Very mobile - Does not require removal of plant parts - Fast testing - Relatively cheap as on device can be used for many plants - No consumables required	- Precision may be limited - Somewhat labour intensive when frequent measurments required	
Growroom installed fixed or mobile optical system	- Can be optimized for conditions in the growroom - Potentially high precision - Frequent sampling possible - No removal of plant samples necessary - Highly automated, low labour cost - No consumables required	- Cost to acquire and install equipment, but potentially cheaper than biochemical laboratory equipment - Bound to the location it has been installed in - New standards and protocols need to be developed in comparison to traditional lab testing	
Dronebased optical system	- Field mobile - Can cover large areas	- Potentially expensive - Likely labour intensive to fly and maintain	

	- No removal of plant samples necessary - No consumables required	- Precision may be affected by environmental factors	

In order to accelerate the development of these instrumentation and test technologies, it is important for scientists across the industry, governmental organisations and academic institutions to come together. For example, a team of New Zealand scientists comprising of academicians, government research agencies and cannabis producers from Rua Bioscience, Callaghan Innovation, SCION, University of Waikato and Unitec Institute of Technology have recently formed. They are working together to develop novel non-destructive optical methods utilising near-infrared (NIR) hyperspectral imaging to capture both the spectral and spatial information of the *Cannabis sativa* flowers as they mature. This information can be correlated with biochemical information gained using current mainstream chemical testing methods to discover the relationships between the optical signals of cannabis plant to the growth conditions cannabinoid-of-interest.

Such initiatives contribute positively to the increasingly wider use of instrumentation and measurement technologies in the context of precision agriculture with the ultimate aim of improving the quality and consistency of plant-based products. In particular to the healthcare industry, this will hopefully be one of many technological solutions towards increasing the global life expectancy, health and well-being.

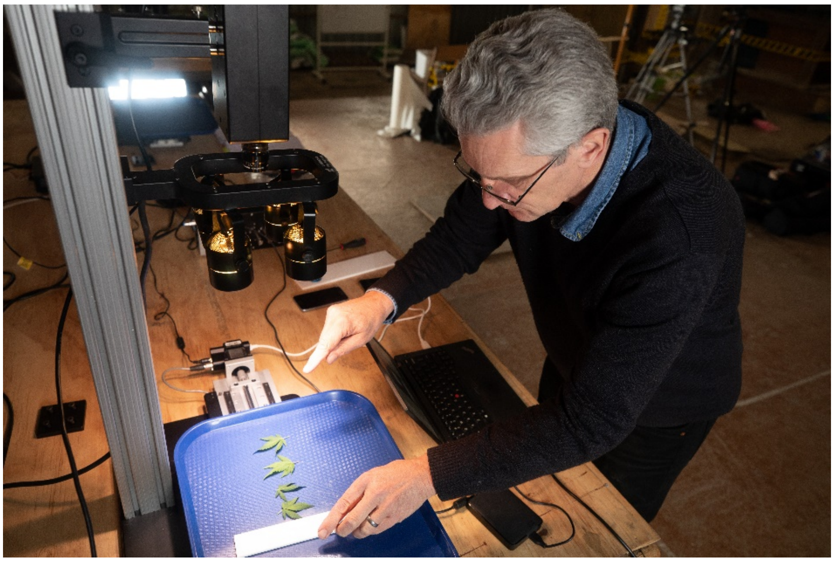

Figure 3: Scientists in New Zealand working to develop optical instruments for cannabis production testing (Source: *Rua Bioscience*)

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