CURCUMIN, CANNABIDIOL, PIPERINE, THC (CANCUR) AS A BENEFICIAL MEDICINAL PRODUCT THROUGH ITS ANTI-EPILEPSY, ANTI-PARKINSON's, ANTI-ANXIETY, ANTI-DEPRESSANT, AND PAIN MANAGEMENT.

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I. ABSTRACT

CURCUMIN is the active component found in Turmeric (Curcuma longa), a respected and well-researched spice long known for medical properties. Turmeric has been in use for thousands of years, while more recent research has shown that Curcumin is the active compound found within. It is used for a wide range of applications, from antioxidant, anti-cancer, anti-inflammatory, arthritis, hyperlipidemia and other related conditions. (Hewlings and Kalman, 2017). It is important to note that Turmeric alone has poor bioavailability and absorption to the human body and that Piperine, a compound found in Black Pepper and Long Pepper has the ability to boost the absorption and bioavailability of Curcumin (Gupta, et.al., 2013).

PIPERINE is an active component found in Pepper, for the purposes of this study, it is mainly used to boost the bioavailability of natural Curcumin. Piperine administrated with Curcumin greatly increases the bioavailability of Curcumin even up to 2000% (Shoba, et.al., 1998).

CANNABIDIOL (CBD)is a generally well-tolerated and non-intoxicating compound found in cannabis that exhibits a range of beneficial properties in a wide range of diseases and disorders. (Kicman, Toczek, 2020) CBD has emerged as a potential prototype for neuroprotective drug development. Its antioxidant and anti-inflammatory behavior help create a neuroprotective effect which helps treat Parkinson's disease, Alzheimer's disease, and other neurodegenerative conditions. (Bhunia, Kolishetti, et.al., 2022).

TETRAHYDROCANNABINOL (THC) is thought to produce the main psychoactive effects of cannabis. However, THC has also been evaluated for medical purposes, as well as interactions with some of the effects of CBD when co-administered. (Boggs, Nguyen, et.al., 2018)

CANCUR is the combination of Curcumin, CBD, Piperine and small amounts of THC. It is a proposed medicinal product that is expected to have anti-epilepsy, anti-Parkinson's, anti-anxiety, anti-depressant, and pain management properties. While there are concerns about the misuse of this product, the dosage involved (0.5 mg THC/capsule) makes it difficult for the psychoactive compound, THC to have detrimental effects on the body.

Keywords: Curcumin, Cannabidiol, CBD, Piperine,1 Tetrahydrocannabinol, THC, turmeric, long pepper, medical cannabis, bioavailability epilepsy, Parkinson's, anxiety, pain, depression, medical properties, Bauertek, The GlobaLeader Inc, Kaibigan sa Kalusugan, CANCUR

II. INTRODUCTION

Turmeric is a plant that grows in Asia and central America, it is also known as the Golden Spice. It gives curry its yellow color and has been used in Ayurveda and traditional Indian medicine to treat various medical and health conditions for thousands for years.

There is a lot of promising research in patients with pro-inflammatory diseases including cancer, arthritis, cardiovascular disease, Chron's disease, Irritable Bowel Disease, psoriasis, diabetes, and many more diseases falling under the same umbrella (Gupta, Patchva, Aggarwal 2013).

Curcumin or diferuloylmethane with chemical formula of (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) and other curcuminoids constitute the main phytochemicals of *Curcuma longa* L. (Zingiberaceae family) rhizome with the common name of turmeric (Zorofchian, Abdul, Hassandarvish,et.al., 2014). However, this research focuses on Curcumin.

Curcumin is the active component of Turmeric, and it has shown that it can modulate multiple cell signaling pathways. Curcumin's activities come from the ability to modulate numerous signaling molecules such as apoptotic proteins, pro-inflammatory cytokines, NF-κB, 5-LOX, STAT3, adhesion molecules, cyclooxygenase-2, C-reactive protein, transforming growth factor-β, prostaglandin E, prostate-specific antigen, phosphorylase kinase, triglyceride, ET-1, creatinine, HO-1, ALT, and AST in human participants (Gupta, Patchva, Aggarwal, 2013).

There is a wide range of therapeutic applications of curcumin, ranging from (and not limited to) Antioxidant, Anti-inflammatory, Hepatoprotective, Antiplatelet aggregation,

Antimutagenic, Antimicrobial, Cardiovascular benefits, topical and local applications on wounds and injuries, Gastric benefits and more. (Nagpal, Sood, 2013)

Curcumin is limited by the poor oral bioavailability as well as its difficulty in solubility in aqueous solutions. This leads to quick systemic elimination, poor absorption, and fast metabolism. (Zorofchian, et. al.,2014) Nagpal and Sood also agree that Curcumin suffers from poor bioavailability along the same lines.

Piperine greatly enhances the bioavailability of Curcumin, increasing bioavailability up to 2000% compared to the limited absorption capacity of Curcumin alone. In more detail, it allowed for greater body absorption within the first hour of post oral intake. (Shoba, et.al., 1998) The low plasma and tissue levels of Curcumin are resolved after a sufficiently proportional amount of Piperine administered together with Curcumin. (Anand, Kunnumakkara, Newman, Aggarwal, 2007).

In general, Piperine helps the body in drug metabolization interactions, as well as intestinal drug absorption. It assists the body with drug metabolizing enzymes and while there are more studies ongoing to uncover the precise pharmacokinetics involved, it is sufficiently proven that it is a beneficial adjuvant to curcumin. (Han, H-K., 2011)

Cannabis, or Marijuana (as it is commonly called) contains a complex mixture of chemicals. Cannabis leaves and buds were traditionally smoked, eaten or even drunk as a form of tea. (Mack, Joy, 2000) One of the chemicals, tetrahydrocannabinol (THC) is the main cause for the high associated with cannabis, while cannabidiol, CBD, the other major compound involved does not cause such effects. (Bhunia, et.al., 2022) Both of these compounds are finding a wider range of medical and therapeutic uses over the recent years. (National Academics Press, US, 2017)

THC or tetrahydrocannabinol is a major component of cannabis and causes psychoactive effects at sufficient doses on the user. Studies on THC have also led to the discovery of the endocannabinoid system in the central nervous system. (Bhunia, et.al., 2022) In 1985, Pharmaceutical companies received approval in the US to develop THC preparations in drugs for therapeutic use (dronabinol and nabilone). Over the last two decades, efforts have been placed into using low-THC/high-CBD products for medical purposes, citing complementary effects for pain, nausea, epilepsy, Parkinson’s disease and many other degenerative and neurological diseases and conditions. (National Academics Press, US, 2017).

CBD or cannabidiol is the non-psychoactive and well-tolerated component found in cannabis. It is gaining popularity due to its benefits over a wide range of diseases, from cardiovascular disorders, liver and kidney benefits, anti-inflammatory and anti-oxidant benefits, as well as its most popular benefits, neuroprotective health benefits. (Kicman, Toczek, 2020) High CBD-low THC products are gaining popularity as multiple states and nations around the world approve of medical cannabis. Chronic pain, neurological diseases, conditions such as Alzheimer’s

disease and Parkinson's disease are some that show promising results among the early generation of users. (National Academics Press, US, 2017)

III. Objectives:

Generally, this study aims to investigate the medicinal potential and health properties of CanCur (Curcumin, CBD, THC and Piperine). Due to legal restrictions for cannabis research and use in the Philippines, the objectives are largely limited to theoretical research until medical cannabis becomes legalized later in 2024. Some parts of this Research and Product Development may have been done in another facility or location where it is legal to do so.

1. Compare the chemical compounds present in CANCUR compared to conventional Turmeric, Cannabis and Pepper;
2. Evaluate the neuroprotective effects of CANCUR for epilepsy, pain management, anxiety, depression and Parkinson's disease.
3. Determine or hypothesize ways to further improve CANCUR.
4. Determine possible major risks of CANCUR.

IV. REVIEW OF RELATED LITERATURE

Turmeric has been long celebrated for its health benefits. In India, it is explained extensively in historical texts such as the Dravyaguna Sastra around two millenia ago. Indians attribute the origin of Turmeric to the Indo-Malayan region, spreading to China around 800 AD and West Africa by 1200 AD. By the 13th Century, Marco Polo wrote about Turmeric in his famous journey. In traditional medicinal systems for both India and China, it has been used for a wide range of diseases such as jaundice, menstrual difficulties, hemorrhage and colic. Even its anti-inflammatory properties have been noted for hundreds of years. (Bora, Deka, Gudade, Shree, 2008) It was also used for a variety of skin disorders, upper respiratory problems, for joint health and digestive system. (NCCIH, 2020)

Today, Turmeric is promoted as a dietary supplement for a wide range of conditions, ranging from digestive disorders to liver disease, arthritis and many others. Most of these supplements are made from dried rhizome and contain small amounts of curcuminoids such as Curcumin. (NCCIH 2020)

Phytoconstituents and Mineral Content

Constituent	Composition (w/w)
Curcuminoids	1–6%
Volatile (essential) oils	3–7%
Fiber	2–7%
Mineral matter	3–7%
Protein	6–8%
Fat	5–10%
Moisture	6–13%
Carbohydrates	60–70%

Figure 5. Estimated Constituent content of an average Turmeric Rhizome. (Nelson, Dahlin, et. al., 2017)

Curcumin is the active component in Turmeric but it isn't the only component found in Turmeric, the figure above shows the usual composition of Turmeric Rhizomes. (Nelson, Dahlin, et. al., 2017) Many fail to fully utilize extracted Curcumin for a more concentrated benefit.

Curcumin has the ability to reduce inflammation, as well as joint pain and stiffness, making it an effective aid for those with arthritis. Even this article agrees with the benefits of taking Curcumin with Piperine, or in a more raw form, Turmeric with Pepper. (Felson, Richmond, 2022)

Other recent studies show the anti-inflammatory benefits of Curcumin that extend to the following diseases such as inflammatory bowel disease, atherosclerosis, COVID-19 and psoriasis. Curcumin exerts anti-inflammatory effects by regulating inflammatory signaling pathways and inhibiting the production of inflammatory mediators. The regulatory effect of Curcumin is beneficial to its treatment of inflammatory diseases. This study also notes the strong antioxidant effects of Curcumin, and how its reduction of ROS (reactive oxygen stress) helps reduce inflammation even further. (Peng, Ao, Dong, Jiang, et.al., 2022)

Cannabis, or Marijuana (as it is commonly called) contains a complex mixture of chemicals. Cannabis leaves and buds were traditionally smoked, eaten or even drunk as a form of tea. (Mack, Joy, 2000) One of the chemicals, tetrahydrocannabinol (THC) is the main cause for the high associated with cannabis, while cannabidiol, CBD, the other major compound involved does not cause such effects. (Bhunia, et.al., 2022) Both of these compounds are finding a wider range of medical and therapeutic uses over the recent years. (National Academics Press, US, 2017)

Cannabis has been increasingly accepted around the world ever since the WHO and the UN pushed for its decriminalization several years ago. (WHO 2020) After the WHO Expert Committee on Drug Dependence (ECDD) concluded that cannabis medicines such as CBD have no potential to be abused and have significant health benefits in cases such as treatment-resistant epilepsy. The WHO also recommended further research and development as well as improved access to cannabis-related medicines to help minimize public health problems related to non-medical cannabis products.

Anti-Oxidant & Anti-Inflammatory Benefits

Studies show that curcumin reduces inflammation by increasing the production of natural cortisone in adrenal glands. (Ammon, Safayhi, et.al., 1993), with curcumin as effective as cortisone or phenylbutazone in acute inflammation, and half as effective in chronic inflammation.(Mukhopadhyay, Basu, Ghatak, 1982)

CBD and THC also exhibit high levels of hepatoprotectivity and antioxidant properties as it also plays an important role in neuroprotectivity. CBD is also noted to be well-tolerated and easy for the body to absorb in low doses, and the recommended dosing of low-THC to high-CBD would be beneficial to exhibit both antioxidant and anti-inflammatory activities.

Pain management

CBD and THC are widely used for chronic pain relief for a variety of uses, ranging from injuries, irritation, post-surgery and even cancer patient relief. (Mack, Joy, 2000) It is also even used in hospice and end-of-life care, when conventional pain treatments fail to work or have too many debilitating side effects. Curcumin is also helpful in pain management as helps with anti-inflammatory benefits as well as provide other beneficial biological activities which may reduce the pain at its source. (Peng, et.al., 2021)

In 2014, 94 percent of Colorado medical marijuana ID cardholders indicated “severe pain” as a medical condition. (Light, et.al., 2014) Likewise, 87 percent of participants in a study looked for medical cannabis for pain relief. This also adds to the growing trend of medical cannabis over conventional pain medications (or even opiates) as a replacement. (Ilgen, et.al., 2013)

One study conducted a Bayesian analysis of five different studies of peripheral neuropathy that tested the efficacy of inhaled cannabis buds. The conclusions towards the five different studies were largely consistent that cannabinoids demonstrated a beneficial effect on pain. (Andreae, et.al., 2015)

A compilation of 28 randomized trials over 2,454 patients with chronic pain showed that the odds for improvement across pain patients were 40% higher than control condition patients across a range of conditions. Said conditions included the following, cancer pain, rheumatoid arthritis, multiple sclerosis, musculoskeletal issues, and chemotherapy-induced pain. (Whiting, et.al., 2015). The effects were consistent over the said range of conditions, and the method of administration was through inhalation.

Epilepsy

Four reports of tests with 48 patients used cannabis monotherapy to reduce incidences of epileptic seizures. The systematic review showed that the overall interval between seizures was three times longer than the previous seizure-free interval. (Gloss, Vickrey, et.al., 2014)

Devinsky (et.al.) reported 162 patients between 1 to 30 years old taking an open-label, expanded access program of oral CBD with no concurrent control group in patients with severe, intractable, childhood onset epilepsy. The median monthly frequency of motor seizures was 30 before taking oral CBD, after a 12-week period, median reduction in motor seizures in these studies was 36.5 percent. (Devinsky, et.al. 2016)

Non-blind tests in Israeli pediatric clinics treating 71 children and adolescents with intractable epilepsy through oral CBD and THC with a 20:1 ratio for six months also showed noticeable improvement. Compared to baseline, the cannabinoid treatment resulted in varying degrees of seizure reduction for the majority of children. Specifically, 18% of children experienced a 75-100% reduction in seizure frequency, while 34% experienced a 50-75% reduction. An additional 12% of children saw a 25-50% reduction, and 26% reported a reduction of less than 25%. However, 7% of children experienced an aggravation of seizures, leading them to discontinue the treatment. (Tzadok, et.al., 2016)

There are other random trials ongoing, but their results have not been published yet, or are unavailable at the moment.

Depression and Anxiety

The endocannabinoid system plays an important role in mood regulation (NIDA, 2015) and cannabis has been explored to determine its connections with Depression and Anxiety.

While trials are limited in scale, a randomized trial with 24 participants with generalized social anxiety disorder were given either placebo or 600 mg cannabinol in a single dose. CBD was associated with a greater improvement in the anxiety factor by a 100- point visual analogue mood scale. The mean difference from baseline being 16.52 points, compared to placebo in a simulated public speaking test. (Whiting, et.al., 2015)

Four other trials with 252 patients were administered dronabinol, 10-20 mg daily, nabilone, maximum 2 mg daily, and nabiximols, 4-48 sprays /day. These trials also supported greater short-term benefits of cannabinoids compared to placebo on self-reported anxiety symptoms. (Whiting, et.al., 2015)

634 participants with various conditions such as chronic pain and multiple sclerosis reported symptoms of depression. Nabiximols, dronabinol and nabilone capsules were compared with placebo in order to combat the effects of depression. While patients report using cannabis for depression, there is still ongoing research to determine the exact cause of cannabis and cannabinoids reducing depressive symptoms. (Whiting, et.al., 2015)

However, randomized tests around the world show a dichotomy of effects. Under moderate cannabis use, depression symptoms decreased in patients. However, heavy use, and overdose led to depression symptoms equal to or higher than that of placebo patients. Thus, a moderate dose of cannabis is recommended to reduce chances of depressive episodes. (National Academies of Sciences, Engineering, and Medicine, 2017)

Parkinson's Disease

While trials are limited in scale, there are different studies which show the effects of CBD and THC in patients with Parkinson's disease. 21 patients were tested with three study arms. Baseline data was compared between 75 mg/day CBD, 300 mg/day CBD and placebo in PDQ-39 (Parkinson's Disease Questionnaire-39) to compare the quality of life. There was a massive improvement of quality of life for patients with 300mg/day of CBD compared (25.57 +/- 16.3) to those under placebo (6.50 +/- 8.48). (Chagas, et.al., 2014)

An open-label study of 22 patients with Parkinson's disease had data collected 30 minutes before and after smoking 0.5 grams or 500 mg of cannabis buds. Total motor syndrome scores were evaluated using the UPDRS, McGill Pain Scale and subjective questions. Under the UPDRS, scores improved from 33.1 to 23.2, while emphasizing significant improvement in rigidity, tremor reduction and bradykinesia. Sleep and pain were also markedly improved after smoking cannabis. (Lotan, Treves, et.al., 2014)

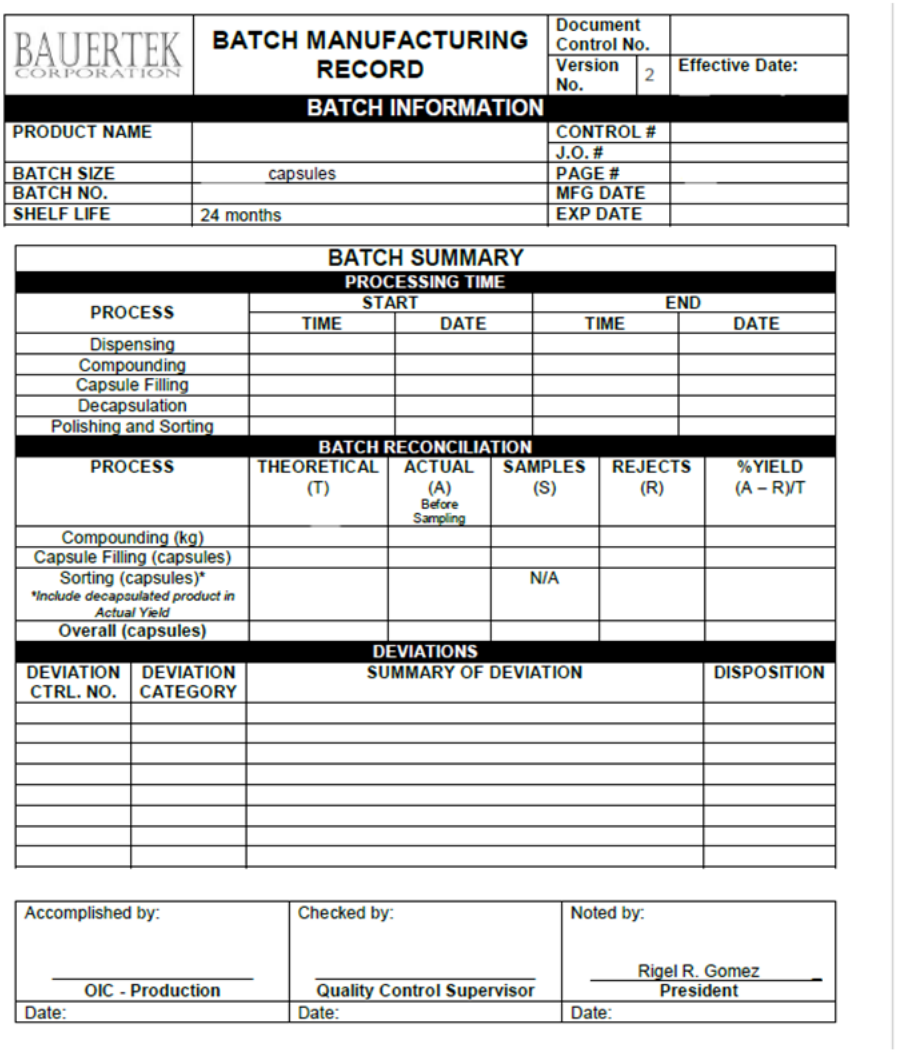
V. METHODOLOGY

The use of cannabis or any derivative materials such as CBD or THC is still a criminal offense under Philippine laws (RA 9125). Therefore this methodology is PURELY THEORETICAL for purposes of the upcoming product development.

A. Theoretical Production of CANCUR

CANCUR will be made through a request from upper management, a Batch Manufacturing Record (BMR) is generated for each batch and steps are detailed in the manufacturing process.

A simplified version of the BMR would be explained here under methodology.



BAUERTEK CORPORATION	BATCH MANUFACTURING RECORD	Document Control No.	
		Version No. 2	Effective Date:

BATCH INFORMATION

PRODUCT NAME		CONTROL #	
		J.O. #	
BATCH SIZE	capsules	PAGE #	
BATCH NO.		MFG DATE	
SHELF LIFE	24 months	EXP DATE	

BATCH SUMMARY

PROCESSING TIME

PROCESS	START		END	
	TIME	DATE	TIME	DATE
Dispensing				
Compounding				
Capsule Filling				
Decapsulation				
Polishing and Sorting				

BATCH RECONCILIATION

PROCESS	THEORETICAL (T)	ACTUAL (A) Before Sampling	SAMPLES (S)	REJECTS (R)	%YIELD (A – R)/T
Compounding (kg)					
Capsule Filling (capsules)					
Sorting (capsules)* *Include decapsulated product in Actual Yield			N/A		
Overall (capsules)					

DEVIATIONS

DEVIATION CTRL. NO.	DEVIATION CATEGORY	SUMMARY OF DEVIATION	DISPOSITION

Accomplished by:	Checked by:	Noted by:
OIC - Production	Quality Control Supervisor	Rigel R. Gomez, President
Date:	Date:	Date:

Figure 1. Sample BMR for CANCUR

The manufacturing process of CANCUR is divided into four stages.

1. Dispensing
2. Compounding
3. Capsule Filling
4. Polishing and Sorting

While decapsulation is listed, it is only for purposes of quality assurance testing and isn't part of the normal processes.

1. **Dispensing**

Theoretical amounts of material are computed in order to make a target batch. These materials are pre-tested for microbes, heavy metal content and also analyzed to ensure these are curcumin, piperine, CBD and THC compounds of suitable quality and purity.

Once Quality Control approves the test results and find them within acceptable parameters in line with FDA standards, these compounds can be taken for Compounding. Quality Assurance starts the monitoring process.

When items are dispensed, it should be in a room that is thoroughly cleaned and disinfected, with set room humidity and temperature as well as negative air pressure to prevent external contamination.

2. **Compounding**

Items ready for compounding are brought to a room with similar standards as dispensing. With a set room humidity, consistent room temperature and negative air pressure to prevent external contamination.

Curcumin, Piperine, CBD and THC are in powdered form, and are sifted through a mesh before being loaded into a compounding machine in an alternating manner.

A 3-D mixing machine will compound the Curcumin, Piperine, CBD and THC together.

Samples are taken from the top, middle and bottom of the mixing vessel, which would be kept in a clean container, to be tested by Quality Control.

Once these materials pass the QC test, this Curcumin, Piperine, CBD and THC compound would then be sent for encapsulation.

3. **Encapsulation**

The compounded Curcumin, Piperine, CBD and THC mix goes to a semi-automatic encapsulation machine, in a room under tightly controlled environment and sanitary conditions.

A semi-automatic encapsulation machine is needed over an automatic machine due to the organic origins of Curcumin, Piperine, CBD and THC, which results to slight variations in the density and characteristics of the Curcumin, Piperine, CBD and THC mix over seasons and

batches. The semi-automatic process allows for more control over quality and easier error detection.

The compounded Curcumin, Piperine, CBD and THC powder are loaded into the encapsulation machine, machine settings are adjusted to match the specifications of the powder and the encapsulation process begins.

Over the course of production, sample capsules are taken every 20 minutes, weight and quality are tested to ensure consistency of the capsules.

4. Polishing and sorting

Once the encapsulation process is completed, capsules are polished through an automated polishing machine. These polished capsules are then taken to the sorting room.

The sorting process is done manually, through visual sorting. Any defective capsules are removed from the batch.

B. Safety Testing

1. HPLC Analysis of Curcuminoids

The extracts will be analyzed analyzed using a Shimadzu Nexera Lite.

Mobile Phase: Tetrahydrofuran and 1 mg/mL of citric acid in water (4:6)

Standard Solution A: 40 µg/mL of USP Curcuminoids RS in Mobile Phase

Standard Solution B: A composite solution containing 40 µg/mL of USP Curcumin RS, 10 µg/mL of USP Desmethoxycurcumin RS, and 2.0 µg/mL of USP Bisdesmethoxycurcumin RS in Mobile Phase. Use sonication if necessary. Before injection, pass through a filter of 0.45-µm pore size, and discard the first 10 mL of the filtrate.

Sample: Use the extracts obtained as is, or dilute with the respective solvent, if necessary, until the area of the Sample peak is less than or roughly equal to the area of the Standard B peaks.

Chromatographic system: The liquid chromatograph is equipped with a Vis detector at 420 nm and a 4.6 x 250 mm 5-µm column with packing L1 (octadecylsilane or C18). The flow rate is set to 1.0 mL/min, and the injection volume is 20 µL.

System Suitability: The chromatogram of Standard Solution A is similar to the reference chromatogram provided with the USP Curcuminoids RS. The resolution between the CUR and DMC peaks, and the DMC and BDMC peaks are NLT 2.0 for Standard Solution B. The tailing factor for the three main peaks are NMT 1.5 for Standard Solution B. The relative standard deviation for the DMC peak is NMT 2.0% for Standard Solution B.

Analysis: Calculate the percentage of CUR, DMC and BDMC extracted from the portion of turmeric powder taken as follows:

$$\%Extracted = \left(\frac{r_u}{r_s}\right) \times C_s \times \frac{1}{D} \times \frac{250}{W}$$

where r_u is the peak area of the relevant analyte from the Sample; r_s is the peak area of the relevant analyte from the Standard Solution B; C_s is the concentration of the relevant analyte from the Standard Solution B; D is the dilution factor, if applicable; and W is the weight of the portion of turmeric powder extracted. Use appropriate statistical and numerical methods to determine the optimum parameters that will result to the maximum extraction yield.

Similar methods are used to determine CBD, THC and Piperine purity and content.

2. AAS Testing of heavy metals

Arsenic Not more than 2.5 ppm

Arsenic in test samples will be analyzed through an Agilent 240 FS Flame Atomic Absorption Spectrometer.

A 1 L 5%HCl + 5%HNO_3 is used as the Dilution solution and stored in an amber glass bottle.

3.0000 +/- 0.0010 g sample is digested by 20 ml concentrated HNO_3 for an hour, after which, 4 ml H_2O_2 is added to the mixture, digesting the sample even further.

The digested material would be diluted in the prepared dilution solution.

A 1000 ppb standard is prepared and diluted into 100 ppb, 75 ppb, 50 ppb and 25 ppb solutions.

An acid and Reductant Solution should also be prepared for the AAS setup.

Once the solutions are ready, the AAS will be prepared for use.

Sampling Mode	Manual
Vapor Mode	Air/Acetylene
Air Flow	13.50
Acetylene Flow	1.50
Measurement Mode	Integration
Measurement Time	5 seconds
Read Delay	90 seconds
Calibration Mode	Concentration
Standard Replicates	3
Sample Replicates	3
Lamp Position	3
Lamp Current	10.0 mA
Wavelength	197.2
Background Correction	BC On
Standard Units	ug/L
Calibration Algorithm	Linear

Figure 2. AAS Settings for Arsenic test

Cadmium Not more than 0.8 ppm

Lead Not more than 0.8 ppm

Lead and Cadmium can be tested together in the same setup. The test samples are analyzed through an Agilent 240 FS Flame Atomic Absorption Spectrometer.

A 1 L 5%HCl + 5%HNO_3 is used as the Dilution solution and stored in an amber glass bottle.

3.0000 +/- 0.0010 g sample is digested by 20 ml concentrated HNO_3 for an hour, after which, 4 ml H_2O_2 is added to the mixture, digesting the sample even further.

The digested material would be diluted in the prepared dilution solution.

A 1000 ppb Pb + 1000 ppb Cd standard is prepared and diluted into 150 ppb, 100 ppb and 50 ppb solutions.

An acid and Reductant Solution should also be prepared for the AAS setup.

Once the solutions are ready, the AAS will be prepared for use.

Instrument Parameter	Lead	Cadmium
Sampling Mode	Autonormal	Autonormal
Instrument Mode	Absorbance	Absorbance
Flame Type	Air/Acetylene	Air/Acetylene
Air Flow	13.50	13.50
Acetylene Flow	2.00	2.00
Measurement Mode	Integration	Integration
Measurement Time	5 seconds	5 seconds
Read Delay	20 seconds	20 seconds
Calibration Mode	Concentration	Concentration
Standard Replicates	3	3
Sample Replicates	3	3
Lamp Position	1	1
Lamp Current	5.0 mA	4.0 mA
Wavelength	217.0	228.8
Background Correction	BC On	BC On
Standard Units	ug/L	ug/L
Calibration Algorithm	Linear	Linear

Figure 3. AAS Settings for Lead and Arsenic test

Mercury Not more than 2.5 ppm

Mercury in test samples will be analyzed through an Agilent 240 FS Flame Atomic Absorption Spectrometer.

A 1 L 5%HCl + 5%HNO_3 is used as the Dilution solution and stored in an amber glass bottle.

3.0000 +/- 0.0010 g sample is digested by 20 ml concentrated HNO_3 for an hour, after which, 4 ml H_2O_2 is added to the mixture, digesting the sample even further.

The digested material would be diluted in the prepared dilution solution.

A 1000 ppb standard is prepared and diluted into 100 ppb, 75 ppb, 50 ppb and 25 ppb solutions.

An acid and Reductant Solution should also be prepared for the AAS setup.

Once the solutions are ready, the AAS will be prepared for use.

INSTRUMENT SETTING	MERCURY
Sampling Mode	Manual
Vapor Mode	Cold Vapor
Measurement Mode	Integration
Measurement Time	5 seconds
Read Delay	90 seconds
Calibration Mode	Concentration
Standard Replicates	3
Sample Replicates	3
Lamp Position	2
Lamp Current	4.0 mA
Wavelength	253.7
Background Correction	BC On
Standard Units	ug/L
Calibration Algorithm	Linear

Figure 4. AAS Settings for Mercury test

Micro-bio Testing

There are four tests to be conducted under Microbio testing, Total Aerobic Microbial Count (TAMC), Total Yeasts and Molds Count (TYMC), Escherichia coli (E. coli) and Salmonella spp.

These are tested under standard guidelines with limits for acceptance criteria set below.

TAMC acceptance criteria is: Not more than 1,000 CFU/g.

TYMC acceptance criteria is: Not more than 100 CFU/g.

E. coli acceptance criteria is: Absent in 25g sample.

Salmonella spp. acceptance criteria is: Absent in 25g sample.

A statistically significant amount of CanCur samples will be taken at different stages, Raw materials, in-process and post-production. Machines and equipment used for production are also regularly tested for contamination.

VI. Health Benefits

While Curcumin, Piperine, CBD and THC (CanCur) has a lot of potential benefits, this paper focuses on its Anti-Epilepsy, Anti-Parkinsons', Anti-Anxiety, Anti-Depressant, and Pain management benefits.

Due to legal limitation, the study on the benefits of Cancur is currently limited up to the review of related literature and methodology. However, once Medical Cannabis is legalized in the Philippines later this year, the methodology to test for health benefits shall be as follows below.

A. Pain Management

Data is collected through an organized process that starts with Free health consultation.

Free health consultation is given to patients with various conditions, where their relevant medical and lab records are taken and recorded, and the appropriate course of action is given.

Recommended dosing of CanCur is given to those whose conditions qualify for CanCur.

Recommended tests are given for a follow-up consultation on a monthly basis, to track the treatment progress.

Tests are taken at accredited (by the Department of Health) laboratory testing centers, clinics or hospitals, and results are compared with previous consultations.

Results are securely stored and noted for future consultation and treatment.

The largest limitation of this method is the voluntary nature of those taking tests, and the relatively wide range of those taking it. While subjects are limited to adult Filipinos, there are few further ways to limit the range of patients aside from dividing by relevant medical condition.

B. Epilepsy

Data is collected through an organized process that starts with Free health consultation.

Free health consultation is given to patients with various conditions, where their relevant medical and lab records are taken and recorded, and the appropriate course of action is given.

Recommended dosing of CanCur is given to those whose conditions qualify for CanCur.

Recommended tests are given for a follow-up consultation on a monthly basis, to track the treatment progress.

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C. Depression and Anxiety

Data is collected through an organized process that starts with Free health consultation.

Free health consultation is given to patients with various conditions, where their relevant medical and lab records are taken and recorded, and the appropriate course of action is given.

Recommended dosing of CanCur is given to those whose conditions qualify for CanCur.

Recommended tests are given for a follow-up consultation on a monthly basis, to track the treatment progress.

Tests are taken at accredited (by the Department of Health) laboratory testing centers, clinics or hospitals, and results are compared with previous consultations.

Results are securely stored and noted for future consultation and treatment.

The largest limitation of this method is the voluntary nature of those taking tests, and the relatively wide range of those taking it. While subjects are limited to adult Filipinos, there are few further ways to limit the range of patients aside from dividing by relevant medical condition.

D. Parkinson's Disease

Data is collected through an organized process that starts with Free health consultation.

Free health consultation is given to patients with various conditions, where their relevant medical and lab records are taken and recorded, and the appropriate course of action is given.

Recommended dosing of CanCur is given to those whose conditions qualify for CanCur.

Recommended tests are given for a follow-up consultation on a monthly basis, to track the treatment progress.

Tests are taken at accredited (by the Department of Health) laboratory testing centers, clinics or hospitals, and results are compared with previous consultations.

Results are securely stored and noted for future consultation and treatment.

The largest limitation of this method is the voluntary nature of those taking tests, and the relatively wide range of those taking it. While subjects are limited to adult Filipinos, there are few further ways to limit the range of patients aside from dividing by relevant medical condition.

VII. RESULTS AND DISCUSSION

The use of cannabis or any derivative materials such as CBD or THC is still a criminal offense under Philippine laws (RA 9125). Therefore the results and discussion portion is still kept blank until further research is permitted.

VIII. PRECAUTIONS, WARNINGS, AND CONTRAINDICATIONS

1.1 Adverse Reactions
The patient is strongly advised to **immediately stop the intake of this product** upon observation of any of the following symptoms/reactions: ▪ Stomach cramps ▪ Nausea ▪ Diarrhea

The patient is advised to consult a physician for medical advice.

1.2 Drug Interactions

The product is proven to have significant pharmacological interactions with the following substances:

- Aspirin
- NSAID painkillers
- Statins
- Diabetes medication
- Blood pressure medication
- Blood thinners
- Cladribine
- Lithium
- Lovastatin
- Ketoconazole
- Itraconazole
- Fexofenadine
- Triazolam
- Etoposide
- Paclitaxel
- Vinblastine
- Vincristine
- Vindesine
- Amprenavir
- Indinavir
- Nelfinavir
- Saquinavir
- Cimetidine
- Ranitidine
- Diltiazem
- Verapamil
- Digoxin
- Corticosteroids
- Erythromycin
- Cisapride
- Cyclosporine
- Loperamide
- Quinidine
- Phenytoin
- Propranolol
- Rifampin
- Theophylline
- Carbamazepine
- Select chemotherapy agents
- Select inhibitors of BCRP

The patient is advised to **disclose all his/her concurrent medication** to a physician and seek medical advice before proceeding with the use of this product.

1.3 High-risk Patient Groups

The following patient groups are at higher risk of experiencing adverse effects:

- Pregnant women
- Lactating Women

If belonging to any one of the aforementioned categories, the patient is strongly advised to consult with a physician before proceeding with the use of this product.

1.4 Laboratory Test Interferences

There is no proof that the product interferes with any laboratory test.

IX. CONCLUSION AND RECOMMENDATION

Based on related literature and studies related to curcumin and medical cannabis, as well as actual trials conducted, several results and recommendations can be made:

1. CANCUR has the potential to manage pain, as well as anxiety and depression.
2. CANCUR also shows promising potential for patients experiencing Epilepsy
3. CANCUR has the potential for neuroprotective capabilities and would be beneficial for patients suffering Parkinson's Disease.

Based on the results, the researchers recommend the following:

1. A more comprehensive study on the uses of CANCUR for pharmaceutical purposes, where a full-scale pharmacokinetic test can be conducted on various patients of different types.
2. A more comprehensive and elucidative study should be conducted to unravel the full potential of CANCUR as a drug. This includes larger scale clinical trials and patients exclusively using CANCUR over the testing period of time.

3. Advocate on the economic and health benefits of CANCUR, allowing for more people to benefit from effective and affordable complementary medicine.
4. More blind tests are recommended in larger scales to prevent biases from affecting the outcome of these studies.

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