CURCUMIN AND PIPERINE (PICUR) AS A BENEFICIAL MEDICINAL PRODUCT THROUGH ITS ANTIOXIDANT, ANTI-CANCER, ANTI-INFLAMMATORY AND OTHER ACTIVITIES

Richard Nixon C. Gomez and Rigel R. Gomez
Bauertek Farmaceutical Technologies Corporation
9001 Kabilang Bakood, Sta. Rita, Guiginto, Bulacan, 3015, Philippines

I. ABSTRACT

CURCUMIN is the active component found in Turmeric (Curcuma longa), a respected and well-researched spice long known for its 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 the plant. It is used for a wide range of applications, from antioxidants, 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 in 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).

PICUR is a combination of Curcumin and Piperine, it has been widely used in the Philippines in the past 14 years as an anti-tumor and anti-cancer supplement. It has been featured in several newspapers and magazines, and in numerous radio broadcasts as well as social media platforms. PICUR's benefits will be assessed through analysis of related literature and consolidated patient lab test results from 2010 onwards.

Keywords: Curcumin, Piperine, turmeric, long pepper, bioavailability, antioxidant, anti-inflammatory, anti-cancer, medical properties.

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 on 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 a 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)

III. OBJECTIVES:

Generally, this study aims to investigate the medicinal potential and health properties of PICUR (Curcumin and Piperine). Specifically, it aims to:

1. Determine the efficacy anti-inflammatory efficacy of PICUR;
2. Compare the chemical compounds present in PICUR compared to conventional Turmeric and Pepper;
3. Evaluate the preventive and cytotoxic effect of PICUR against inflammation, tumors and its observed effects on cancer patients.
4. Determine or hypothesize ways to further improve PICUR.

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 millennia 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, various forms of cancers, 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 rawer 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)

Antioxidant & Anti-Inflammatory Benefits

While observation from our local testing is still ongoing, there are numerous reports of reduced swelling in cases of muscle pain, Osteo Arthritis, Rheumatoid Arthritis, and similar cases.

Other related 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)

Anti-Tumor & Anti-Cancer Benefits

Curcumin shows potential in both prevention and treatment for cancer (Mehta, Pantazis, McQueen, Aggarwal, 1997). It inhibits metastasis of cancer cells and works to stop carcinogenesis in three stages; Tumor promotion (Kawamori, Lubet, Steele, 1999), angiogenesis (Thaloor, Singh, Sidhu, Prasad, et.al., 1998) and tumor growth (Limtrakul, Lipigorngoson, et.al.,1997).

In several studies of colon and prostate cancer, curcumin inhibited tumor growth and cell proliferation. And in other cases, it also prevents new cancers from developing after chemotherapy and radiation therapy, reducing the chances of relapse. (Mehta, Pantazis, et.al., 1997)

Antioxidant and free-radical reduction capabilities and their ability to indirectly increase glutathione levels also aid in the hepatic detoxification of carcinogens and mutagens, as well as inhibiting the formation of nitrosamine. (Dorai, Cao, et.al., 2001)

V. METHODOLOGY

A. Production of PICUR

PICUR is 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	Curcumin + Piperine (PICUR) 250mg Food Supplement Capsule	CONTROL #	
		J.O. #	
BATCH SIZE	capsules	PAGE #	
BATCH NO.	PC-	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 PICUR

The manufacturing process of PICUR 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 analyzed to ensure these are curcumin and piperine compounds of suitable quality and purity.

Once QA and QC approve of the test results and find them within acceptable parameters in line with FDA standards, these compounds can be taken for Compounding.

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.

Piperine and Curcumin 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 Piperine and Curcumin 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 and Piperine compound would then be sent for encapsulation.

3. Encapsulation

The compounded Curcumin and Piperine mix go 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 and Piperine, which results to slight variations in the density and characteristics of the Curcumin and Piperine mix over seasons and batches. The semi-automatic process allows for more control over quality and easier error detection.

The compounded Curcumin and Piperine 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 encapsulation process is completed, capsules are polished through an automated polishing machine. These polished capsules are then taken to the sorting room.

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 are 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 Bisdemethoxycurcumin 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.

2. AAS Testing of heavy metals.

Arsenic Not more than 2.5 ppm

Arsenic in test samples is 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 is 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 conducted under Micro-Bio 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 PiCur samples are 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 and Piperine (PiCur) has a lot of potential benefits, this paper focuses on is Antioxidant and Anti-inflammatory benefits, as well as provide a preliminary investigation on Anti-tumor and anti-cancer benefits.

A preliminary study is being conducted to confirm PiCur's health benefits, it is divided into two forms, Antioxidant & Anti-Inflammatory, and Anti-Tumor & Anti-Cancer.

A. Antioxidant & Anti-Inflammatory Benefits

Since inflammation can be easily observed checked through clinical observation, comments of medical practitioners and feedback from patients are used in the evaluation process.

B. Anti-Tumor & Anti-Cancer Benefits

Data is collected through an organized process done in 14 Health Clinics in the Philippines. Collection is done on a weekly basis, and has been going on for the past 14 years.

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

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

Recommended tests are given for a follow-up consultation monthly, to track the treatment progress. These tests include but not limited to: Tumor marker tests (CA15-3, CEA, CA125, CA199, CA72-4, PSA), Imaging (Ultrasound, CT-Scan, PET Scan, MRI, Xray, Bone Scan), and other relevant tests.

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.

There are numerous reports of reduced inflammation and better general comfort after taking PiCur. This includes reduction of tumor size, quantity, and improvement of tumor quality. Patients with BIRADS 6 (Malignant) Breast Tumors were observed to have improvements up to BIRADS 2 (Benign) and BIRADS 1 (no tumor). Similar cases are also observed on patients with Prostatomegaly, thyromegaly, and many other cases.

Observed local cases include the obvious reduction of blood vessels around the tumors (stops angio-genesis and/or vascularization). Tools used include Ultrasounds, CT Scans, and MRIs.

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

1. Production of PICUR

Batch #	Quality control	Distributed
1	PASS	YES
2	PASS	YES
3	PASS	YES
4	PASS	YES

2. Safety Testing

a. HPLC Testing

Batch #	Curcumin content > 95%	Piperine Content > 95%
1	PASS	PASS
2	PASS	PASS
3	PASS	PASS
4	PASS	PASS

b. AAS Testing

Batch #	Arsenic below 2.5 ppm	Cadmium below 0.8 ppm	Lead below 0.5 ppm	Mercury below 2.5 ppm
1	PASS	PASS	PASS	PASS
2	PASS	PASS	PASS	PASS
3	PASS	PASS	PASS	PASS
4	PASS	PASS	PASS	PASS

c. Microbio Testing

Batch #	TAMC below 1,000 CFU/g	TYMC below 100 CFU/g	E. coli absent in 25 g sample	Salmonella spp. absent in 25 g sample
1	PASS	PASS	PASS	PASS
2	PASS	PASS	PASS	PASS
3	PASS	PASS	PASS	PASS
4	PASS	PASS	PASS	PASS

3. Anti-Tumor& Anti-Cancer Benefits

PiCur shows remarkable benefits among those with cancer (malignant tumors) and non-cancer related (benign tumors). Out of over 10,000 cases selected for the study, most cases (over 70%) showed either a reduction in tumor size and weight, or a reduction in cancer marker related statistics, such as CA15-3, CEA, CA125, CA199, CA72-4 and PSA statistics. Those that did not show a marked improvement were also highly likely to not follow the dosing and other recommendations given.

The cases selected were all taken from patients with tumors.

The patients are all adult Filipinos, from 30 years old above, both male and female.

The main limitation of the study is the voluntary nature of patients. There are differences in dosing, where patients with more severe cases take higher doses of PiCur. Some patients were also advised to take conventional medical treatments while being administered PiCur, to increase their chances of survival and recovery. Another limitation would be the limited ability of the researchers to constantly monitor said patients taking PiCur.

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. PiCur should be take 2 hours away from any of these drugs.

1.3 High-risk Patient Groups

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

- Those with hyper-acidity
- Those with gastric ulcerations

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

1. PICUR shows clear results in reducing tumors as well as reducing cancer cells, as noted in cancer marker tests.
2. PiCur best utilizes the Antioxidant and Anti-Inflammatory benefits of Curcumin, through the application of Piperine to increase its bioavailability.
3. PiCur works with most conventional treatments to help fight cancer, its ability to prevent cancerous cell growth, redirecting cell lines as well as increasing hepatoprotectivity makes it an ideal companion for chemotherapy, radiation therapy and surgery, to increase chances of survival.

Based on the results, the researchers recommend the following:

1. A more comprehensive study on the uses of PICUR 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 PICUR as an antioxidant and an anticancer drug. This includes larger scale clinical trials and patients exclusively using PICUR over the testing period of time.
3. Test other ways to increase bioavailability of Curcumin, including utilizing supercritical extraction and nano processing, as well as how it can work together with Piperine. This may help the body absorb Curcumin even better for stronger health benefits.
4. Advocate on the economic and health benefits of PICUR, allowing for more people to benefit from effective and affordable complementary medicine.

X. LITERATURE CITED

1. Hewlings, S. J., & Kalman, D. S. (2017, October 22). Curcumin: A review of its' effects on human health. [PMC]. National Institutes of Health (.gov). Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5664031/

2. Subash C Gupta, Sridevi Patchva, & Bharat B Aggarwal (2013). Therapeutic roles of curcumin: lessons learned from clinical trials. Retrieved from https://pubmed.ncbi.nlm.nih.gov/23143785/

3. Shoba, G., Joy, D., Joseph, T., Majeed, M., Rajendran, R., & Srinivas, P. S. (1998). Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. Planta Medica, 64(4), 353-356. Retrieved from https://pubmed.ncbi.nlm.nih.gov/9619120/

4. Nagpal, M., & Sood, S. (2013). Role of curcumin in systemic and oral health: An overview. Journal of Indian Society of Periodontology, 17(1), 3–7. [PMC3633300] [PubMed]

5. Nelson, K. M., Dahlin, J. L., Bisson, J., Graham, J., Pauli, G. F., & Walters, M. A. (2017). The essential medicinal chemistry of curcumin: Miniperspective. Journal of Medicinal Chemistry, 60(24), 11203-11218.

6. Zorofchian Moghadamtousi, S., Abdul Kadir, H., Hassandarvish, P., Tajik, H., Abubakar, S., & Zandi, K. (2014). A review on antibacterial, antiviral, and antifungal activity of curcumin. *BioMed Research International, 2014*, 186864. https://doi.org/10.1155/2014/186864

7. Anand, P., Kunnumakkara, A. B., Newman, R. A., & Aggarwal, B. B. (2007). Bioavailability of curcumin: Problems and promises. *Molecular Pharmaceutics, 4*(6), 807-818. https://doi.org/10.1021/mp700113r

8. Han, H-K. (2011). The effects of black pepper on the intestinal absorption and hepatic metabolism of drugs. *Expert Opinion on Drug Metabolism & Toxicology, 7*(6), 721-729. https://doi.org/10.1517/17425255.2011.570332

9. Bora, S. S., Deka, T. N., Gudade, B. A., & Shree, A. B. R. (2008, August). Nutrition corner, turmeric special. *PMFME Newsletter*. Ministry of Food Processing Industries. https://www.pmfme.mofpi.gov.in/newsletters/enewsaugust8/article1.html

10. National Center for Complementary and Integrative Health (NCCIH). (2020, May). Turmeric. https://www.nccih.nih.gov/health/turmeric

11. Felson, S. (Reviewer), & Richmond, C. (Author). (2022, January 23). Health benefits of turmeric [Slideshow]. WebMD. https://www.webmd.com/diet/ss/slideshow-turmeric

12. Peng, Y., Ao, M., Dong, B., Jiang, Y., Yu, L., Chen, Z., Hu, C., & Xu, R. (2021). Anti-inflammatory effects of curcumin in the inflammatory diseases: Status, limitations and countermeasures. *Drug Design, Development and Therapy*, 15, 4503-4525. https://doi.org/10.2147/DDDT.S327378

13. Ammon, H. P. T., Safayhi, H., Mack, T., & Sabieraj, J. (1993). Mechanism of anti-inflammatory actions of curcumin and boswellic acids. *Journal of Ethnopharmacology, 38*(2-3), 113-119.

14. Mukhopadhyay, A., Basu, N., & Ghatak, N. (1982). Anti-inflammatory and irritant activities of curcumin analogues in rats. *Agents Actions, 12*(4), 508-515.

15. Mehta, K., Pantazis, P., McQueen, T., & Aggarwal, B. B. (1997). Antiproliferative effect of curcumin (diferuloylmethane) against human breast tumor cell lines. *Anticancer Drugs, 8*(5), 470-481.

16. Kawamori, T., Lubet, R., Steele, V. E. (1999). Chemopreventative effect of curcumin, a naturally occurring anti-inflammatory agent, during the promotion/progression stages of colon cancer. *Cancer Research, 59*(3), 597-601.

17. Thaloor, D., Singh, A. K., Sidhu, G. S., Prasad, P. V., Kleinman, H. K., & Maheshwari, R. K. (1998). Inhibition of angiogenic differentiation of human umbilical vein endothelial cells by curcumin. *Cell Growth & Differentiation, 9*(4), 305-312.

18. Limtrakul, P., Lipigorngoson, S., Namwong, O., Apisariyakul, A., & Dunn, F. W. (1997). Inhibitory effect of dietary curcumin on skin carcinogenesis in mice. *Cancer Letters, 116*(2), 197-203.

19. Dorai, T., Cao, Y. C., Dorai, B., Buttyan, R., & Katz, A. E. (2001). Therapeutic potential of curcumin in human prostate cancer. III. Curcumin inhibits proliferation, induces apoptosis, and inhibits angiogenesis of LNCaP prostate cancer cells in vivo. *Prostate, 47*(4), 293-303.