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Addition of The Modified Turmeric Extract (*Curcuma longa* L.) to Food and its Functional Effect on Cancer-Related Liver Inflammations

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FUNCTIONAL foods containing active ingredients have anti-inflammatory properties that modulate inflammation in chronic diseases, particularly hepatitis associated with cancers treated with chemotherapy, which are a worldwide concern due to the liver's importance in the detoxification process, but these active ingredients face poor bioavailability. Curcuminoids, the active compounds in the *C. longa* plant, have recently been identified as beneficial for improving the functional value of food, but their distribution is difficult due to their poor ability to dissolve, meaning much of their effectiveness is lost. The study's first goal is to improve the solubility, stability, and color intensity of turmeric dry extract during food processing by vigorously grinding it with sodium bicarbonate and second, is converting the dry turmeric extract particles into nanoscale to increase its anti-inflammatory properties. According to the findings, adding sodium bicarb changes the curcuminoids into their salts and reduce their molecular size (approximately 155.2 nm), which enhances their stability, water solubility and color intensity. Modified turmeric extract (MTE) was added to crackers at three different concentrations as a functional food additive. The cracker samples were investigated for sensory evaluation, which indicated general acceptance of all attributes. The effect of addition of MTE alone or in combination with cisplatin in cracker samples on the levels of IL-6 in the HepG2 cell line was (1.60±0.22 µg/mL and 2.31±0.34 µg/mL, respectively) when compared to cisplatin was used alone (3.74±0.51 µg/mL).Overall, this approach to MTE nano-form may be a promising strategy for its use as a functional food that helps cancer-related liver inflammation cases.

Keywords: Functional food, Modifiedturmeric,Curcuminoids nanoparticles, Interleukin 6, Crackers.

Introduction

Chemotherapy is commonly associated with side effects such as increased inflammatory markers, especially those in the liver, as the liver plays a major role in the detoxification process and is also responsible for the intermediate metabolism of nutrients such as proteins, glucose, and fatty acids (Bonala et al,. 2020). One of the top priorities in cancer control is to provide effective, low-cost health therapies that can significantly reduce mortality and disability. Because 85% of chemotherapy patients develop hepatitis as a side effect, which can progress to hepatic steatosis, the most serious condition, controlling chemotherapy side effects is critical. As a result, the world's focus is shifting to nature in search of new treatments that do not have negative side effects, as chemotherapy does. Numerous studies have revealed that many natural sources, such as medicinal and aromatic plants, contain bioactive compounds that can be used as natural antioxidants and can reduce these effects (Li et al., 2021). Active components in medicinal

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and aromatic plants have therapeutic effects as antioxidants, anti-allergic and anti-cancer agents. They have the ability to inhibit the synthesis of inflammatory mediators like cyclooxygenase (COX)-2 and cytokines (Heendeniya et al., 2018; Wagner et al., 2003). Among the most important of these components are phenolic compounds, which are considered an essential category of food additives for their role in reducing fat oxidation in foodstuffs, increasing shelf life, preserving sensory and nutritional properties, and providing therapeutic value to the product (Ramadan, 2013).

Functional foods or supplements are foods that contain ingredients that provide health benefits in addition to their nutritional value, as these foods help maintain health and thus reduce the chance of disease. Studies have indicated that vegetarian diets are beneficial in the treatment of fatty liver disease (FLD) (Li et al., 2021).One of the most important medicinal and aromatic plants that has therapeutic capabilities is *Curcuma longa* (Turmeric), which belongs to the family *Zingiberaceae* and has many traditional uses, such as its use as an additive to improve food quality and taste, as well as being an important antioxidant. Turmeric has gained popularity recently due to its multiple pharmacological properties, as it contains chemically and biologically active substances such ascurcumin , desmethoxycurcumin, and bisdemethoxycurcumin (Hefnawy et al., 2016). However, turmeric is difficult to dissolve in water, which limits its effectiveness. The main objective of the current study was to add sodium bicarbonate to increase solubility, enhance color, and spread more effectively during the manufacturing process of functional foods containing turmeric. In addition to the previous objectives, this study also aimed to supplement modified turmeric (in the form of functional food) and study its effect on chemotherapy-related hepatitis in induced tumor cells *in vitro*. Crackers were chosen as the application model because they are one of the most popular baked goods among consumers, have a high nutritional value, are inexpensive, and have a long shelf life.

Materials and Methods

Chemicals.

Turmeric powder and almost commercially ingredient including wheat flour was used for baking, fat and sodium bicarbonate, ammonium bicarbonate, salt, skim milk powder and sugar powder used for baking were obtained from local markets (Cairo, Egypt). Pure curcuminoid with purity (95%) HPLC grade was obtained from EL-Goumhouria Co. Chemical and Medical Department 23 EL SawahStr, Cairo, Egypt. Lipopolysaccharide stock (LPS) was manufactured by Siga Chemical Co. (St. Louis, Mo, USA) and purchased from the Egyptian International Center for Import Cairo, Egypt. Cisplatin (Cis-DiamineDichloro-Platine II) (50 mg, vial) was manufactured by Agila Specialties Pvt. Ltd., Bangalore, India and purchased from EL-Ezaby Pharmacy, Cairo, Egypt.

Preparation of turmeric powder extract (TE)

Turmeric powder (200 g) was homogenized in a blender with 1000 mL of 80% ethanol for 2 h at 60 °C. The extract was centrifuged at 6500 x g for 10 min. at 4 °C, and the supernatant was filtered through filter paper (No. 3, 110 mm, Whatman). Turmeric extract (TE) filtered solution was concentrated using a rotary evaporator under reduced pressure at 60 °C to remove ethanol. The TE (yield 30%, w/w) was freeze dried, and stored at 4°C until required (Scheme 1).

Determination of proximate compositions of turmeric powder

The contents of moisture, dry matter, protein, crude fiber, and the total amount of ash were measured by AOAC (2000). The fat content of the sample was determined by Pearson (1976).

Determination of phytochemicals (qualitative and quantitative)

Alkaloids, sterols, and flavonoids were determined by the method described by Haborne (1998). Saponins were determined by the method described by AOAC (2000). Phenol and Tannins were determined by the method described by Person (1976).

Preparation of modified turmeric extract (MTE).

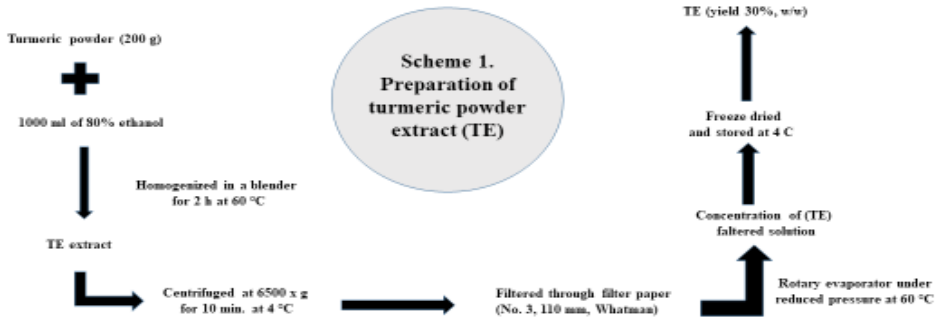
The modified turmeric extract MTE was prepared by mixing TE powder with sodium bicarbonate 1:1(w/w) by using a strong blinder with a speed of 4500 rpm until the colour of the mixture turns from yellow to dark orange (from 5 to 10 min) (scheme 2 and picture 1).

Particle size characterization,pH value, and FT-IR

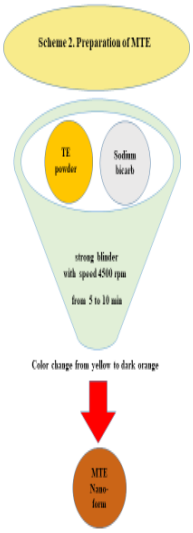
Particle size analysis and FT-IR were provided by Applied Chemistry Department – Egyptian Petroleum Institute, Cairo, Egypt.

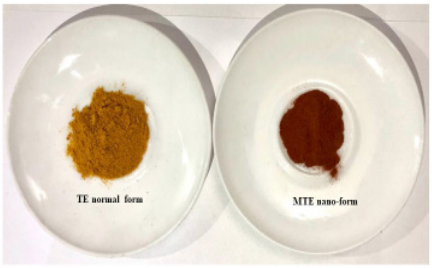
Determination of pH value

A pH electrode (pH meter) is used to measure the pH forgottenand solutions (10 mL of extract powder: 100 mL distilled water). A measure of the pH of a solution expressed as a number on a scale from 0 to 14.



Scheme 1.





Picture 1. Difference in color between turmeric extract (TE) and modified turmeric extract (MTE) nano-form

Particle size characterization

The particle diameter of turmeric extract before modification and turmeric extract after (MTE) were determined by Dynamic light scattering instrument (Nano ZS, Malvern Analytical, U.K.). Both samples were prepared by taking 1 mg of powder in 10 mL of distilled water.

FT-IR analysis

To make translucent sample discs, 10 mg of the dried nanoparticles sample was encapsulated in 100 mg of KBr pellet and exposed to a pressure of around 5x106 Pa in an evacuated die to generate a clear transparent disc with a diameter of 13 mm and a thickness of 1mm. At room temperature, IR spectra in the range of 4000-400 $cm^{-1}$was acquired using a Perkin Elmer Fourier transform spectrometer (FT-IR) with an air cooled DTGs (deuterated tri-glycine sulphate) detector. CO was added to 100 images of each spectrum at a spectral resolution of $4cm^{-1}$. All sharp bands' frequencies were accurate to 0.01 cm^{-1}(Organic spectroscopy principles and applications, 2005).

In Vitro evaluation of MTE cytotoxicity

To determine the MTE cytotoxicity effect on HCC cells,the MTT assay was done according to Wagner, 2003 published technique to perform the test. HCC cells (5 × 103 cells/well) were seeded in 96-well microplate in triplicates, incubated overnight, and treated with MTE from 0 to 50 µg/

mL. Cisplatin was added in the range of 0 to 32 µg/mL concentrations for comparing its cytotoxic activity with TME. After incubation for 48 h, 20 µL of MTT reagent (5 mg/mL) was included in each well-following incubation at 37 °C for 24 hr. Next, the culture medium was carefully removed and replaced with the addition of 200 µL of DMSO for complete solubility of formazan crystals. The absorbance was read at 570 nm by using an Elisa plate reader (Sun et al., 2019).

Crackers preparation

Crackers were made by whisking 90 grams of sugar with 60 g of fat for 5 minutes to form cream. The cream was mixed for 5 minutes with water containing ammonium bicarbonate (3 g) as well as sodium chloride (3 g) while replacing the amount of sodium carbonate associated with modified turmeric is considered during manufacture, then the mixture was divided into two parts: The first part, control sample, 150 g of wheat flour sieved twice, mixed for 3 minutes with baking powder (0.9 g). In the second part, treated samples, 150 g of wheat flour was sieved twice, and mixed for 3 minutes with baking powder (0.9 g), then this part was divided again into three parts to add MTE with three different concentrations according to IC_{50}value. The doughs were sheeted to 3.5 mm thickness, cut into circular shapes using a 45 mm template, placed on an aluminum tray, cooked at 160 ºC for 10 minutes, and then left to cool. The cracker samples were kept at room temperature in closed dark containers (Sulieman et al., 2019).

Physical and chemical properties of crackers

According to Adebowale et al.(2012), the moisture and ash content of cracker samples were determined. Also, physical characteristics such as weight, width, and thickness were measured in cracker samples enhanced with MTE.

Sensory evaluation of crackers

Crackers samples were evaluated organoleptically by 10 trained panelists according to Bajaj et al., (2006). The tested characteristics included: Colour, Crumb colour, Texture, Taste, and Overall accessibility. All sensory items were evaluated through 10 marks.

Determination of MTE anti-inflammatory on marker IL-6

To determine MTE anti-inflammatory effect on inflamed liver cells treated with cisplatin according to the IC_{50} obtained, the in -vitro inflammatory model was induced in HepG2 cells by treating the cells with 1µg/ mL of lipopolysaccharide (LPS) for 48 hours. After cells grew overnight,cells were divided into the normal control group (NC), HepG2-induced inflammation group (PC), and HepG2-induced inflammation + Cisplatin group (Cis), HepG2-induced inflammation + cisplatin+ MTE group (Cis + MTE) and HepG2 induced inflammation + cisplatin+ MTE cracker samples extract group (Cis + MTE-CSE). The cells were then incubated for an additional 48 h prior to their use in the evaluation of IL-6 values using enzyme-linked immunosorbent assay kits [Shanghai Enzyme-linked Biotechnology Co., Ltd., Shanghai, China], according to the manufacturer's instructions(Jing et al., 2012).

Statistical analysis

Results were analyzedby ANOVA using the SAS (1999) statistical package of the general linear model (GLM). The results averages were based on a three-replicates ($p \leq 0.05$) (SAS Statistical Analysis System, 1999).

Results and Discussion

Consumption of functional foods in the form of snacks was on the rise as a result of civilizational progress and the trend towards all that is natural. The production of nutritional supplements has become associated with this development and is desirable for various age groups, especially when it is characterized by a low production cost. Turmeric (*Curcuma longa*) has the golden main ingredient known as curcumin. It is a polyphenol that is used for many purposes, for example as a spice, food coloring and traditional herbal remedy. It has been proven that the phenolic compound curcumin has many benefits with a therapeutic effect, as it improves brain function, helps in weight loss, controls the level of sugar when taken by a diabetic, and has anti-inflammatory, anti-cancer, and antioxidant properties. However, curcumin in its natural form loses a large part of its therapeutic capabilities due to its poor water solubility and low bioavailability, especially when used orally. In this study, turmeric extract (curcuminoids) was modified by adding sodium bicarbonate to turn into its salts and become more alkaline. Also, its particle size was reduced to the nanoscale, which enhanced its stability and water solubility. MTE's biological activity as an anti-inflammatory agent was tested in vitro on HepG2-induced inflammation models to see how a modified turmeric extract as a part of a functional food ingredient affects hepatic inflammation markers associated with chemotherapy and how it can be used as a functional food.

Proximate and Phytochemical analysis of turmeric

Proximate analyses were performed todetermine the numerous benefits that turmeric plants possess. The result s in Table 1 showthe commercial turmeric powder sample contains 8.9% moisture, 2.9% ash, 4.0% crude fiber and 6.71% fat. It also contains 8.8% crude protein and 68.4% carbohydrate. The results of the analysis show that turmeric extract can be a great source of both protein and carbohydrates. The ash content of 2.9% in turmeric indicates that it contains a significant amount of minerals that play a significant role in raising the efficiency of the immune system. The fiber (6.71%) included in turmeric will help to clean the digestive system by removing free radicals from the body and avoiding the absorption of too much cholesterol, which in the case of elevated levels could cause inflammation (Ikpeama et al.,2014).

Qualitative and quantitative phytochemical screening emphasizes the pharmaceutical values of the turmeric plant. As shown in Table 2, positive results were obtained in terms of alkaloids (0.73%), saponins (0.49%), tannins (1.10%), sterols (0.04), phenols (0.09), and flavonoids (0.42%). The presence of these phytochemicals confirmed the turmeric plant's medicinal value, Saponins (0.49%) is a type of glycoside that has soap-like characteristics. Saponins have anti-inflammatory properties that complement turmeric's therapeutic value. Saponins have been shown to have beneficial properties such as lowering cholesterol and eliminating harmful bodies by causing cytotoxic effects via intestinal permeability (Enemor et al., 2020). Tannins (1.10%) possess antibacterial properties. Tannins are water-soluble plant polyphenols that precipitate proteins (Kasta, 2020). Because turmeric contains alkaloids (0.73%), it can be used to treat hypertension-related headaches, as well as colds, persistent mucus, and migraines. Furthermore, due to the presence of saponins (0.49%) and flavonoids (0.42%), the turmeric plant may be useful in the management of inflammation, improving sex hormone, decreasing cholesterol, avoiding harmful cytotoxins, and having antioxidant properties (Ikpeama et al.,2014). The phytochemical analysis of the extract reveals that it contains 0.42% flavonoids that have a number of biological actions, one of which is their ability to scavenge for biological radicals and superoxide anion radicals, which makes them beneficial to health. Flavonoids have anti-inflammatory, analgesic, anti-allergic, and antioxidant properties. These findings support the use of the turmeric plant to treat a variety of diseases and it is strongly recommended as one of the most important nutritional supplements (Kasta, 2020).

MTE particle size and stability

This step was performed to ensure that if there

TABLE 1. Proximate analysis of Methanolic turmeric plant .

Item 1.1.1.1.1.	**%** 1.1.1.1.2.
Moister 1.1.1.1.3.	**8.90**
Total ash	**2.90**
Crude fiber	**4.70**
Total protein	**8.80**
Total fat	**6.70**
Total carbohydrates	**68.0**

TABLE 2. Qualitative and quantitative phytochemical screening of Methanolic TE.

Phytochemicals	Qualitative	Quantitative %
Alkaloids	**+ ve**	**0.73**
Anthraquinones	**- ve**	**-**
Cardiac glycosides	**- ve**	**-**
Flavonoids	**+ ve**	**0.42**
Phenols	**+ ve**	**0.09**
Saponins	**+ ve**	**0.49**
Sterols	**+ ve**	**0.04**
Tannins	**+ ve**	**1.10**

is any noticeable difference between TE and MTE particle size. The particle size of turmeric extracts before modification (TE) and turmeric extracts after modification (MTE) were studied using dynamic light scattering (DLS), and the distributions of the hydrodynamic diameter of the synthesized particles are shown in Figure 1 (A and B). The hydrodynamic radius of turmeric extracts before modification is (664.6 nm), whereas the hydrodynamic radius of turmeric extracts after modification (MTE) is approximately (155.2 nm). This result indicates that the new method of preparing turmeric extract by grinding it hard with sodium bicarbonate has aided in reducing particle size, transformed turmeric extract particles into the nanoscale, increased the speed of its dissolution in water, and made it more stable when compared to the standard extract.We found that the addition of sodium bicarbonate helped change the pH from 7.02 to 9.0; curcumin's color changed from yellow to dark orange (Picture 1).

The stability of MTE particles, such as color, turbidity, and sediment, was observed visually for 2 weeks after mounting under +4 °C. Also, no change in color (orange) was observed, the turbidity was stable, and negligible particles were found in sediment at the bottom of the vials during the storage period.

The size of nanoparticles influences therapeutic and diagnostic applications by influencing therapeutic delivery factors such as circulating half-life, target cellular uptake, and tumor penetration. Medical nanotechnology has aided in the development of nanoparticles capable of reaching their intended target by determining the optimal size based on therapeutic goals, disease location, and other nanoparticle properties. To avoid passing through the renal filtration barrier, nanoparticles should be larger than 10 nanometers and smaller than 200 nanometers to avoid stimulating the complement system and accumulating in the liver and spleen (Hoshyar et al., 2016; Pérez-Campaña et al., 2013). Therefore the size obtained for MTE particles(155.2 nm) is reliable within the biologically active nanoscale as shown in Figure 1 (A and B). When compared to the standard extract, the new method of preparing turmeric extract by grinding with sodium bicarb has aided in particle size reduction, transformed turmeric extract into the nanoscale form, increased the speed of its dissolution in water, and made it more stable. Therefore, it should be noted that the purpose of using only the zeta particle analysis was to determine whether the new method of modified turmeric preparation affected the size particle measurements of turmeric extract or not, and this was confirmed by the previous results.Curcuminoid products in nanoscale sizes are believed to have better particle distribution within the product than in its natural form, as the distribution factor is one of the most important determinants of stability and other desirable properties, such as deliciousness and biological performance, such as improved oral absorption of entrapped nutrients(Pérez-Campaña et al., 2013).

FTIR analysis

FTIR spectroscopy is considered the best analytical approach for qualitative and quantitative studies (Rohman et al., 2015). Table 3 lists the functional groups responsible for the infrared absorption of the curcuminoid nanoparticles in the MTE sample calibrated with a curcuminoid standard. Finally, the wavenumbers of 1400-1720 cm^{-1} were preferred for quantification of curcumin CUR, wavenumbers of 1480-1746 cm^{-1} used for quantitative analysis of desmethoxycurcumin DMCUR, the combined wavenumbers region of 1170-1226 cm^{-1} and 1470-1785 cm^{-1} used for analysis of bisdemethoxycurcumin BDMCUR, while the wavenumbers of 1400-1820 cm^{-1} were exploited for analysis of total curcuminoid. These results wear confirmed by Rohman et al. (2015) and Wulandari et al. (2018). It is known that the curcuminoids in the ethanolic extract of *C. longa* are the predominant phenolic compounds that give turmeric its yellowish color. As shown by the obtained results, this step was a procedure to ensure that the majority of the ethanolic extract of the modified turmeric MTE was curcuminoids.

MTE cytotoxicity effect (IC_{50})

Figure 2 shows the cytotoxic effects of modified turmeric extract MTE on the hepatocellular carcinoma HCC cells in comparison to cisplatin as a standard drug. From the results, it could be noticed that the concentration that induced 50% inhibition in cell cancer growth (IC_{50}) was found to be 4.6 g/mL for cisplatin and 4.7 g/mL for MTE. According to these results obtained in figure 2, after observing the effect of each drug on the HCC model, there is a decrease in the level of cells growth in the two groups treated with cisplatin (4.6 µg/mL) and MTE (4.7µg/mL). However, we thought that MTE was more effective and safer in this inhibition process than cisplatin, which is known to have severe side effects on both healthy and cancerous cells (Abdel-Hamid et al., 2022; Zhang et al., 2019).

Chemical and physical properties of crackers

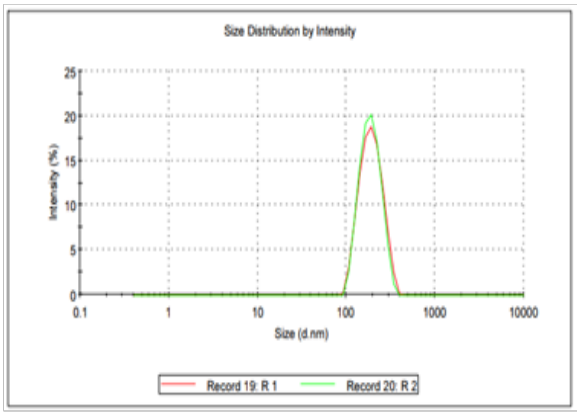


Fig. (1 A). DLS-measured size distribution of turmeric extracts TE before modification (664.6 nm).

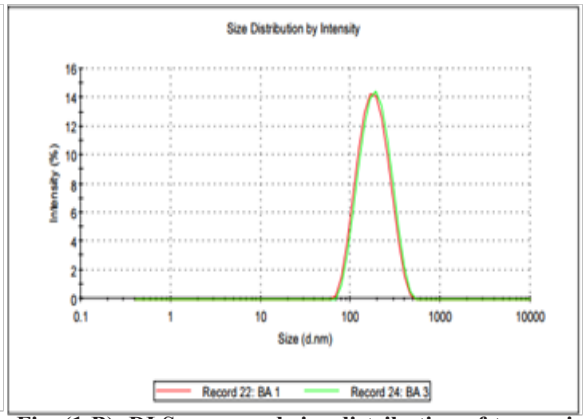


Fig. (1 B). DLS-measured size distribution of turmeric extracts after modification MTE (155.2 nm).

TABLE 3. Functional groups responsible for infrared absorption of curcuminoid nanoparticles in MTE sample.

Wave numbers (cmG1)	Functional groups
3508	-OH stretching vibration
3050	C-H aromatic stretching vibration
2960	-CH3-asymmetric stretching
2920	-CH2 asymmetric stretching
1630	C = O stretching
1626	C = C aromatic stretching
1512	Benzene ring bending vibration
1505	CH2 bending
1338	CH3 bending
1030	C-OH stretching

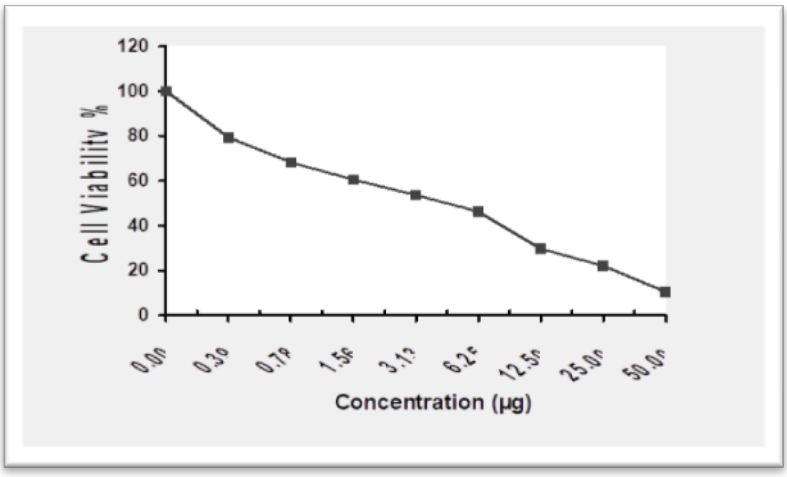


Fig. 2. Inhibitory activity of modified turmeric extract MTE against the HCC model on HepG2 was detected under these experimental conditions with IC_{50} 4.7 µg/mLl for MTE.While cisplatin standard gives Inhibitory activity against the HCC model was IC_{50} = 4.6 µg/mL.

MTE cracker samples were prepared in three different treatments based on the MTE cytotoxicity value and then tested for chemical, physical, and sensory evaluation. The samples contained less moisture than control crackers, according to the results obtained in Table 4. The ash content of crackers containing MTE was increased from 1.24 ± 0.01% in control samples to 1.26 ± 0.01% in MTE (A sample) and 1.27 ± 0.01% in MTE (B and C samples), respectively. Weight, width, thickness, and MTE crackers were all evaluated, and the outcomes are presented in Table 5. The weight of the MTE crackers was lower than that of the control sample, which had the highest weight (9.8 g). The data showed that the moisture content was gradually decreasing. This could be due to the high water binding with other ingredients in the MTE-enriched cracker formulation. The decrease in moisture content in MTE samples may have good effects on microbiological quality and processed cracker sample texture (Nanditha et al., 2009). The ash content of crackers containing MTE was comparable to that of the control; according to the findings of this study, the ash values increased slightly from (1.24±0.01%) in control samples to (1.26± 0.01%) in MTE (A sample) and 1.27 ±0.01% in MTE (B and C samples), respectively. The weight of the control sample was the greatest (9.8 g), whereas the weight of MTE crackers was less. The width of the MTE samples was comparable to the control. Because of the addition of sodium bicarb, the thickness of the MTE samples was greater than the control (Yildiz et al., 2019). The present study indicates that the physical parameters of crackers were influenced by the added MTE treatments. This could be due to the interaction of the MTE formulation with various ingredients during baking processing (Hefnawy et al., 2016).

Sensory evaluations of crackers

Ten qualified panels assessed the sensory evaluation of the cracker samples. As shown in Table 6, the MTE samples were well accepted in terms of color, crumb color, and texture and were comparable to the control. According to the findings, the addition of MTE has no effect on the sensory parameters of crackers, but it does improve the acceptability of cracker samples. Sensory evaluation plays an important role in evaluating food quality because it determines the general acceptability of the consumer. The most important basic quality characteristics evaluated in this study were color, crumb color, taste, texture, and overall acceptability. Turmeric as a spice is the primary ingredient in curries but can also be an ingredient used as a flavoring in many food products including juices, beverages, and baked products. The overall accessibility of control samples and MTE samples had the same degree of acceptance (Table 6). The results indicated that the three concentrations of MTE in the crackers had satisfactory overall accessibility and that the volatile substances and phenolic compounds did not adversely affect the taste of the tested samples(Giri et al., 2020; Yildiz et al., 2019).

7. In vitroevaluation of MTE (crackers) as an anti-inflammatory functional food product.

It is well understood that there is a direct link between the food we eat and our health. Thus, in addition to being essential to the proper and normal functioning of the human body, functional components of food can also be used proficiently in the treatment and prevention of certain diseases such as liver inflammations. An important immune and inflammation factor of interest to study due to its wide range of immunomodulatory and hematopoietic activities, as well as its potent ability to induce an acute phase response, is IL-6, which is a multifunctional cytokine that plays an important role in host defense. Interleukin 6 (IL-6) appears to be a viable target for autoimmune diseases and plays a role in the pathogenesis of several human diseases. In this study, the related inflammation in the HepG2-induced inflammation model exposed to cisplatin, MTE, and MTE crackers extracts were observed in the current study by evaluating the inflammatory marker IL-6, as shown in Table 7. The HepG2-induced model treated with TME + cisplatin (TME + Cis) recorded a significant reduction in IL-6 values (1.60± 0.22), with no significant difference with the normal control (1.55±0.38) and a significant difference with the cisplatin (Cis) alone (3.43 ±0.48), while the HepG2-induced model treated with cisplatin (Cis) recorded a significant increase in IL-6 values (3.43 ±0.48) with no significant difference with the positive control (3.74 ±0.51), however TME-CE + cisplatin (TME-CE + Cis) recorded a moderate significant reduction in IL-6 values (2.31±0.34) with significant difference with the cisplatin (Cis) alone. According to previous results, using modified turmeric extract MTE alone or as part of a functional food product significantly reduces IL-6 as an inflammatory factor, especially if used along with chemotherapy, making it suitable for use as a functional food

targeted at cases of inflammation linked to cancer brought on by chemotherapy.

Cisplatin is toxic because it accumulates inside the cell, attaches directly to the cell›s DNA, and causes destructive cell damage (Zhang et al., 2019). This pro-inflammatory cytokine as IL-6 serves as a marker for acute inflammatory responses, such as liver fibrosis and other ROS-related diseases. Cisplatin has also been shown to cause direct liver damage through a mechanism involving membrane rigidity and activation of oxidative stress processes, which in turn stimulate cytokines and thus motivate inflammatory processes (Yarijanietal, 2018; Gorabietal, 2021). The purpose of this study was to see how a modified turmeric extract in its nano-form affects cisplatin-induced hepatitis. According to the study, TME which can be taken as a food supplement or as part of functional food ingredients, has more positive side effects than chemotherapy drugs like cisplatin, protects cells from oxidative and inflammatory factors through antioxidants and anti-inflammatory derivatives, and also improves the action of cancer chemotherapy drug, particularly when used as a complementary therapy. This activity has been linked to the medicinal properties of the turmeric components.

Conclusion

TABLE 4. Moisture and ash content (weight %).

Sample	Moisture	Ash
Control	4.4 ± 0.09	1.24 ± 0.01
MTE (a)	4.1 ± 0.02	1.26 ± 0.01
MTE (b)	4.0 ± 0.02	1.27 ± 0.01
MTE (c)	3.8 ± 0.07	1.27 ± 0.01

Values represent the mean ± S.E.M. (n = 3), with significant different at ($p < 0.05$)

TABLE 5. Physical parameters of crackers.

Sample	Weight (g)	Width (mm)	Thickness (mm)
Control	9.8 ± 0.14	58.7 ± 0.12	5.8 ± 0.16
MTE (a)	7.6 ± 0.10	58.9 ± 0.12	6.0 ± 0.11
MTE (b)	7.4 ± 0.12	59.0 ± 0.13	6.2 ± 0.11
MTE (c)	7.4 ± 0.12	59.0 ± 0.13	6.5 ± 0.12

Values represent the mean ± S.E.M. (n = 3), with significant different at ($p < 0.05$)

TABLE 6. Sensory characteristics of crackers.

Sample	Color	Crumb color	Texture	Taste	Overall accessibility
Control	7.5 ± 0.09	8.1 ± 0.10	8.0 ± 0.15	7.8 ± 0.15	7.9 ± 0.09
MTE (a)	8.2 ± 0.14	7.8 ± 0.10	7.7 ± 0.13	8.0 ± 0.10	7.7 ± 0.10
MTE (b)	8.3 ± 0.12	7.5 ± 0.13	8.4 ± 0.12	8.1 ± 0.08	7.7 ± 0.10
MTE (c)	8.4 ± 0.12	7.4 ± 0.13	8.5 ± 0.12	8.1 ± 0.08	7.5 ± 0.10

Values represent the mean ± S.E.M. (n = 3), with significant different at ($p < 0.05$)

TABLE 7. IL-6 Inflammatory mediator levels measured in cultured media for HCC model on HepG2cells after treatment with IC_{50} of tested extract.

Group	IL-6 (µg/mL)
(NC)	1.55±0.38
(PC)	3.74±0.51
(Cis)	3.43±0.48
(TME+ Cis)	1.60±0.22
(TME-CE + Cis)	2.31±0.34

Values represent the mean ± S.E.M. (n = 5), with significant different at ($p < 0.05$)

NC: Normal Control, PC: Positive Control, Cis: Cisplatin, TME: Modified Turmeric Extract, TME-CE: TME crackers extract.

The current study focused on the new method of preparing MTE in its nano-form as an anti-inflammatory agent for hepatitis, especially in cancer-related conditions, and its application in functional food to improve their general health. The results showed that MTE (which can be taken as a food supplement or as part of functional food ingredients) combined with chemotherapy can protect cells from chemotherapy-induced hepatitis. MTE treatment significantly reduced the levels of IL-6, an important inflammatory marker, in tumor cells. Crackers containing MTE were accepted as functional foods, and all of their organoleptic properties were tested and found to be satisfactory. This approach of MTE may be a promising strategy for its use as a functional food in several products, as future biological and histological studies will prove. MTE nanoparticles have the potential to be an effective adjuvant and a natural platform for cancer treatment.

Recommendations

The study directors recommend that the method for preparation of MTE in its nano-form be adopted as an approved new method.

Declaration of Conflicting Interests

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Abbreviations

TE	**Turmeric Extract**
MTE	Modified Turmeric Extract
CUR	Curcumin
DMCUR	Desmethoxycurcumin
BDMCUR	Bisdemethoxycurcumin
(COX)-2	Cyclooxygenase
FLD	Fatty Liver Disease
IL-6	Interleukin 6
FT-IR	Fourier Transform Spectrometer
Cis	Cisplatin
NC	Normal Control
PC	Positive Control

References

Abdel-Hamid, N. M., EL-Gharieb, M. S., El-Senduny, F. F.and Alnakib, N. (2022) Assessment the effect of Cisplatin and Doxorubicin on Nitric Oxide levels on HepG2 cell line. *Alfarama JournalofBasicand Applied* Sciences, **3**(2), 220-229.https://doi.org/10.21608/ajbas.2022.104013.1074

Adebowale, A. A., Adegoke, M. T., Sanni, S. A., Adegunwa, M. O.andFetuga, G. O. (2012). Functionalpropertiesandbiscuitmakingpotentialsof sorghum-wheat flour composite. *American Journal of food technology*, **7**(6), 372-379.https://doi.org/ 10.3923/ajft.2012.372.379

Bajaj, S., Urooj, A.andPrabhasankar, P. (2006) Effect of incorporation of mint on texture, colour and sensory parameters of biscuits. *International Journal of Food Properties*, **9**(4), 691-700.https://doi.org/10.1080/10942910600547632

Bonala, S., Gupta, M. K.andVadde, R. (2020) Functional foods in the prevention of colorectal cancer. *Critical Reviews™ in Oncogenesis*, **25**(2).https://doi.org/10.1615/CritRevOncog.2020035112.

Enemor, V. H. A., Ogbodo, U. C., Nworji, O. F., Ezeigwe, O. C., Okpala, C. O.andIheonunekwu, G. C. (2020) Evaluation of the nutritional status and phytomedicinalproperties of dried rhizomes of turmeric (Curcuma longa). *Journal of Biosciences and Medicines*, **8**(8), 163-179.https://doi.org/10.4236/jbm.2020.88015

Giri, N. A., Sajeev, M. S.andKrishnakumar, T. (2020) Development and physico-chemical evaluation of protein rich cookies using underutilized Curcuma aungustifolia starch. *Journal of Pharmacognosy and Phytochemistry*, **9**(6S), 91-97.

Gorabi, A. M., Razi, B., Aslani, S., Abbasifard, M., Imani, D., Sathyapalan, T. andSahebkar, A. (2021) Effect of curcumin on proinflammatory cytokines: A meta-analysis of randomized controlled trials. *Cytokine*, **143**, 155541.https://doi.org/10.1016/j.cyto.2021.155541

Harborne, A. J. (1998) Phytochemical methods a guide to modern techniques of plant analysis. Springer science & business media.

Heendeniya, S. N., Ratnasooriya, W. D.andPathirana, R. N. (2018) In vitro investigation of anti-inflammatory activity and evaluation of phytochemical profile of Syzygiumcaryophyllatum. *Journal of Pharmacognosy and Phytochemistry*, **7**(1), 1759-1763.

Hefnawy, H. T., El-Shourbagy, G. A.and Ramadan,

M. F. (2016) Phenolic extracts of carrot, grape leaf and turmeric powder: antioxidant potential and application in biscuits. *Journal of Food Measurement and Characterization*, **10**(3), 576-583.https://doi.org/10.1007/s11694-016-9339-7

Hoshyar, N., Gray, S., Han, H.andBao, G. (2016) The effect of nanoparticle size on in vivo pharmacokinetics and cellular interaction. *Nanomedicine*, **11**(6), 673-692.https://doi.org/10.2217/nnm.16.5.

Ikpeama, A., Onwuka, G. I.andNwankwo, C. (2014). Nutritional composition of Tumeric (Curcuma longa) and its antimicrobial properties. International Journal of Scientific and Engineering Research, 5(10),1085-1089.https://doi.org/10.4236/vp.2020.64020

Jing, Y. Y., Han, Z. P., Sun, K., Zhang, S. S., Hou, J., Liu, Y.and Wei, L. X. (2012) Toll-like receptor 4 signaling promotes epithelial-mesenchymal transition in human hepatocellular carcinoma induced by lipopolysaccharide. *BMC Medicine*, **10**(1), 1-12. https://doi.org/10.1186/1741-7015-10-98

Kasta, G. (2020) Antimicrobial activity of ethanol extract of rhizome turmeric (Curcuma longa L.) for growth of Escherichia coli, Staphylococcus aureus and Candida albicans. *Asian Journal of Pharmaceutical Research and Development*, **8**(3), 5-8.https://doi.org/10.22270/ajprd.v8i3.712

Li, H. Y., Gan, R. Y., Shang, A., Mao, Q. Q., Sun, Q. C., Wu, D. T.and Li, H. B. (2021) Plant-based foods and their bioactive compounds on fatty liver disease: Effects, mechanisms, and clinical application. Oxidative medicine and cellular longevity, 1, 6621644. https://doi.org/10.1155/2021/6621644

Nanditha, B. R., Jena, B. S. and Prabhasankar, P. (2009) Influence of natural antioxidants and their carry through property in biscuit processing. Journal of the Science of Food and Agriculture, 89(2), 288-298.https://doi.org/10.1155/2021/6621644

Official Methods of Analysis (2000) 17th Ed., AOAC INTERNATIONAL, Gaithersburg, MD, Appendix D

Organic spectroscopy principles and applications (2005) 2nd Edn, Narosa publishing House, Daryagani, Delhi**.**

Pérez-Campaña, C., Gómez-Vallejo, V., Puigivila, M., Martín, A., Calvo-Fernández, T., Moya, S. E. and Llop, J. (2013) Biodistribution of different sized nanoparticles assessed by positron emission tomography: a general strategy for direct activation of metal oxide particles. *ACS nano*, **7**(4), 3498-3505.https://doi.org/10.1021/nn400450p

Person, D.(1976) Chemical analysis of foods. 7th edition. Edinburgh Churchill stone**.**

Ramadan, M. F. (2013) Healthy blends of high linoleic sunflower oil with selected cold pressed oils: Functionality, stability and antioxidative characteristics. *Industrial Crops and Products*, **43**, 65-72.https://doi.org/10.1016/j.indcrop.2012.07.013

Rohman, A., Ramadhani, D.and Nugroho, A. (2015) Analysis of curcumin in Curcuma longa and Curcuma xanthorriza using FTIR spectroscopy and chemometrics. *Research Journal of Medicinal Plant*, **9**(4), 179-186. https://scialert.net/abstract/?doi=rjmp.2015.179.186

SAS Statistical Analysis System, SAS/STAT User's Guide (1999) Release 6.03 Ed. SAS Institute, Cary, NC, 1028 p**.**

Sulieman, A. A., Zhu, K. X., Peng, W., Hassan, H. A., Obadi, M., Siddeeg, A.and Zhou, H. M. (2019) Rheological and quality characteristics of composite gluten-free dough and biscuits supplemented with fermented and unfermented Agaricusbisporus polysaccharide flour. *Food Chemistry*, **271**, 193-203.https://doi.org/10.1016/j.foodchem.2018.07.189

Sun, C., Li, W., Liu, Y., Deng, W., Adu-Frimpong, M., Zhang, H.and Xu, X. (2019) In vitro/in vivo hepatoprotective properties of 1-O-(4-hydroxymethylphenyl)- -L-rhamnopyranoside from *Moringa oleifera* seeds against carbon tetrachloride-induced hepatic injury. *Food and Chemical Toxicology*, **131**, 110531.https://doi.org/10.1016/j.fct.2019.05.039

Wagner, I., Greim, C., Laufer, S., Heide, L. and Gleiter, C. H. (2003) Influence of willow bark extract on cyclooxygenase activity and on tumor necrosis factor-alpha or interleukin 1 beta release in vitro and ex vivo. *Clinical pharmacology and therapeutics*, **73**(3), 272-274.https://doi.org/10.1067/mcp.2003.32

Wulandari, R., Martono, S.and Rohman, A. (2018) Liquid chromatography and Fourier transform infrared spectroscopy for quantitative analysis

of individual and total curcuminoid in Curcuma longa extract. *Journal of Applied Pharmaceutical Science*, **8**(9), 107-113.https://doi.org/10.1067/mcp.2003.32

Yarijani, Z. M., Godini, A., Madani, S. H.and Najafi, H. (2018) Reduction of cisplatin-induced renal and hepatic side effects in rat through antioxidative and anti-inflammatory properties of Malvasylvestris L. extract. *Biomedicine and Pharmacotherapy*, **106**, 1767-1774.https://doi.org/10.1016/j.biopha.2018.07.115

Yildiz, E. L. i. F., Gungor, G., Yilmaz, H.and Gocmen, D. (2019) Changes in bioaccessibility, phenolic content and antioxidant capacity of novel crackers with turmeric (Curcuma longa L.) and mahaleb (Prunusmahaleb L.) powders. *Quality Assurance and Safety of Crops & Foods*, **11**(2), 107-116.http://dx.doi.org/10.3920/QAS2018.1334

Zhang, X., Jin, L., Tian, Z., Wang, J., Yang, Y., Liu, J.and He, Y. (2019) Nitric oxide inhibits autophagy and promotes apoptosis in hepatocellular carcinoma. *Cancer science*, **110**(3), 1054-1063. https://doi.org/10.1111%2Fcas.13945