Detection of Biological Activity of *Curcuma longa* Methanol Extract and Its Antibacterial effect on *Staphylococcus aureus*.

Covenant Ogbonna^{1*}, Erkey Özgör^{2,3}

Abstract

Plants are known to possess enormous profound benefits, which if well incorporated in daily living have the potential to influence our health in ways unexpected. Significant progress has been made concerning the anti-oxidative and anti-cancerous effect of bioactive components in food products, worthy of note in the curcuminoids derived from turmeric (*Curcuma longa*) rhizomes. Therefore, to this end, this research aims to describe succinctly the phytocomponents, antioxidant activity and antimicrobial activity of turmeric methanol extract. The zones of inhibition were measured after plating on a Mueller Hinton agar plate and compared to the standards penicillin G and chloramphenicol. Chloramphenicol used as a positive control was found to be most effective on *Staphylococcus aureus* while *Curcuma longa* methanol extract and penicillin G were found to have the same microbial inhibition due to the negative control. Compared to the IC₅₀ values of Ascorbic acid which was 5 mg/ml, *Curcuma longa* methanol extract had a lower IC₅₀ value is 3.2 mg/ml which according to previous literature is a good one given that lower IC₅₀ values indicate great antioxidant activity. It was gathered by the observation that the qualitative extraction of *Curcuma longa* using methanol shows the presence of varying chemical components such as AR-tumerone, arachinsaeure, alpha-tumerone amongst others. Research data suggest that ar-tumerone has the potential to promote the positive and negative proliferation of tumor cell lines. As a result, *Curcuma longa* has high potential to be developed into an antibiotic against Methicillin-resistant *Staphylococcus aureus* and other clinically important bacterial strains in future.

Keywords: *Curcuma longa*, antimicrobial activity, antioxidant activity, *Staphylococcus aureus*

Introduction

Plants are known to possess enormous profound benefits, which if well incorporated in daily living have the potential to influence our health in ways unexpected. However, it is worthy of note that certain plant components are known to be comprised of esters, inorganic and organic components, in some cases hydrocarbons which play a role in increasing the vitality of the human system. Certain plants are known to possess increased antioxidant activity, antimicrobial activity, carminative effects, repair of dead cells, ability to boost cardiovascular stability.

Fiber is of great importance in metabolic activity of our digestive system, and our overall health by improving blood cholesterol, abating lung and colon cancer and the prevention of diseases like diabetes. Over time, fibers have been obtained from husks of corn, stalks of cotton, straws of wheat, barley and rice and peels of plantain or banana, citrus husks amongst others (1). *Curcuma longa* is a resourceful member of the *Zingiberaceae* family. Turmeric identified botanically as *C. longa* is often cultivated for the importance of its rhizomes, however, the plant produces a substantial amount of leaves and stem from which oil and other extractives are derived (2).

Turmeric is mostly consumed as a yellow powdered spice with an aesthetic flavor and

¹Cyprus International University, Department of Bioengineering, 99258, Nicosia, Mersin 10, TURKEY

²Cyprus International University, Department of Molecular Biology and Genetics, 99258, Nicosia, Mersin 10, TURKEY

³Cyprus Bee and Bee Products Research Centre, Cyprus International University, 99258, Nicosia, Mersin 10, TURKEY

*Corresponding author: e-mail: covenantsdg2017@gmail.com
phone: +90 3926711111, fax: +90 3926711122

DOI: 10.2478/ebtj-2021-0009

© 2021 Authors. This work was licensed under the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 License.

medicinal prowess capable of preserving the freshness of the product prepared. In traditional medicinal practices, turmeric has been used in its various forms to combat one or more health conditions ranging from stomach aches, to use as a blood purifier to the treatment of skin anomaly. However, the predominant application of turmeric is observed and described as antimicrobial, anticancer, antitumor, wound healing, venom antidotes and also hepatic-protective (3).

Only recently analyzed anti-oxidative potential in food products become a thing of worldwide acceptance and interest. Significant progress has been made in relation to anti-oxidative and anti-cancerous effect of bioactive components in food products, worthy of note in the curcuminoids derived from turmeric rhizomes (4).

Worthy of note is the attribute of turmeric which makes it a dye for artistic representation, for textile products, for use in drugs against cancer, dermatitis, AIDS. With regards to the significance which bioactive constituents in herba naturale wield, there is an ever-growing discontent with better extraction methods and detailed means of phenotyping these components. To this effect, various spectrometric methods have sufficed including the HPLC-MS, GC-MS amongst others (5).

The composition and volatility of *Curcuma longa* extracts is the basis of the characteristic smell moreover, fixed phenolic compounds like curcumin are a requisite for their intense yellow color (6). A wide input of clinical studies on standardized curcumin has described beneficial pharmacological effects and plausible functional food ingredient or therapeutic agent (7).

The rhizome is about 2-10 cm in length, cylindrical, ovoid, branched and deep in orange color. A recent report on methanol extract of a species of turmeric shown a significantly strong antifungal activity besides its known anti-bacterial activity (8). In general, essential oils from *Curcuma spp.* are complex mixtures of sesquiterpenes, monoterpenes and aromatic compounds, which have been shown strong antioxidative, anti-inflammatory and anti-bacterial activities. Germacrone can also inhibit the proliferation of MCF-7 by inducing cell cycle arrest and triggering apoptosis (9).

Organic extracts of turmeric prevent curtailed DNA sabotage. The anti-inflammatory and antioxidant effects of this natural rhizome according to several studies appear to inhibit cancer induced by the cell cycle. Besides tumerone, curcumin is also an active agent in turmeric for in treating several types of cancer examples include breast cancer and lung cancer, by promoting cancer cell death, through curtailed immune responses in form of inflammation, and slowing down tumor growth. It also contains (Superoxide dismutase 1 (SOD1)), which has proven potential to prevent cancerous cell development in the prostate as well as to inhibit secondary melanoma, the tumor of the brain, amongst others (10). One of the bottlenecks in the application of turmeric as a therapeutic agent is that it can be easily metabolized or broken down within the body which could result in double bonds in the reduction of di-bonds in heptadienedione chain. A secondary outcome of this will be the production of the active metabolite (11).

Many researchers have pointed out the ability of turmeric to exhibit anticancer activity with a dual-phase pattern which affects the proteasome, such that at decreased doses of application there will be higher inhibitory effects. As is rightly known, inhibition of proteasome has the potential to induce cell death however, its stimulation could also provoke cell stimulation for survival even though this is largely dependent on the application dosage. Cumulatively, various application doses of the turmeric extract could result in alternative cell death options, this is to say that low application doses might affect the pattern of apoptosis and oxidative stress, while the higher application doses might lead to reduced availability of ROS species (12).

Therefore, to this end, this research aims to describe succinctly the phytochemical components, antioxidant activity and antimicrobial activity of turmeric (*Curcuma longa*) methanol extract.

Materials and Methods

2.1 Preparation of *Curcuma Longa* methanol extract

All plant materials (dried powdered turmeric rhizomes) which are grown on a farm in Nicosia, Cyprus (Lat-Long: 35.050179, 33.716818) were collected, cleaned, freeze-dried at -80°C and ground into a fine powder by grinder. The method adapted for this extraction was as described by Kutti Gounder and Lingamallu (3). Turmeric (*Curcuma longa*) rhizome powder extract was prepared by mixing 50 g of powdered leaf in 400 ml HPLC grade methanol in an Erlenmeyer flask and stirred for 48 hours on an overhead shaker at room temperature kept in boiling water bath for 10 min. The extract was filtered through Whatman filter paper No.5 and stored in the refrigerator. The extract was recovered by the use of a rotary evaporator at 40 rpm at a temperature of 50°C for an hour. The dry mass of extracts was stored for further use.

2.2 Gas chromatography-mass spectrometry

The different solvent extracts were analyzed by gas chromatography-mass spectrometry (GC-MS) according to certain conditions (13). The GC or GC-MS conditions were optimized based on the property of the various solvent extract. HP-5 fused silica capillary column (30 m×0.25 mm, film thickness 0.25 µm). Helium (purity 99.99%) was used as the carrier gas, with a flow rate of 0.9 mL/min. The column oven temperature was programmed from 50°C (hold 1 min) to 240°C (hold 10 min) at a 5°C/min rate. *C. longa* methanol extracts injected in an Agilent 7890A GC system coupled with an MS (Agilent technologies) by author injection at the environmental laboratory, Cyprus International University. The operating conditions of the GC-MS set for the analysis were as follows: oven temperature was set at 50°C for 2 min then 100°C at 10°C/min and steadily increased to 200°C and held at a constant temperature for 10 min. The sample injection volume was 2 µL and the carrier gas was helium at 1 mL/min. The ionization of the sample components was carried out 70 eV. The total time of the GC analysis was 24.50 min for *C. longa* methanol extracts.

2.3 DPPH Free radical-scavenging ability

The DPPH radical-scavenging activity was determined using the method shown by Tavares et al. (6). 100 μ M DPPH was dissolved in pure methanol (96%). The stock solution was prepared fresh. The DPPH solution 3 ml was added to 1 ml of *C. longa* methanol extracts across the quintuplet concentrations. The mixture was shaken and allowed to stand at 37°C for 10 min in the dark. The decrease in absorbance of the resulting solution was calculated for 10 min at 517 nm with ELISA Reader. The results were corrected for dilution and expressed in mg/ml. All determinations were performed in duplicate.

2.4 Antimicrobial assessment by disc diffusion plate method

Curcuma longa methanol extracts for antimicrobial tests were centrifuged and filtered with sterile 0.45 μ m microfilter. *Staphylococcus aureus* (ATCC 6538 P), was serially diluted with nutrient broth and incubated for 24 hours at the optimum temperature of 37°C. Briefly, Mueller Hinton agar plates were prepared by weighing out grams of the powdered media and dissolving in distilled water then autoclaved at 121°C at 15psi for 15mins. After which the sterile media is aseptically poured into 60mm petri dishes and allowed to dry before the experiments. Standard antibiotic concentrations chloramphenicol (1 mg/ml) were used as a positive control for the sake of this while for the negative control DMSO (0.9%) solution prepared. Also, McFarland standard as a basis for the preparation of the bacterial suspension sequel to which 200 μ l of the suspension was added to the agar plate and spread evenly onto the agar surface. 6 mm discs were loaded with 30 μ l of *C. longa* methanol extracts and incubation was done for 24hrs at 37°C. The areas or diameter of inhibition was observed and measured in the units of a millimeter (mm). Every process was performed aseptically in duplicates. After the disc diffusion method, SPSS 16 software was used for statistical evaluation of zone diameters (in millimeters) measurement data. The effectiveness of *C. longa* was evaluated with the Duncan test for *S. aureus*.

Results

3.1 Gas chromatography-mass spectrometry

Table 1 shows the occurrence of the various bioactive compound as observed by different organic solvents. Some compounds were in increased occurrence depending on the solvent of choice.

3.2 DPPH Free radical-scavenging ability

The DPPH radical-scavenging activity evaluated to detect the antioxidant capacity of *C. longa*. Antioxidants over time have found relevance in many ways ranging from additives to preservatives to combat oxidative degradation of food. There are a variety of synthetic chemicals which possess radical scavenging ability, however alongside their positive effect lies their negative effect which poses a bottleneck to their advancement of application (5). The human race more than ever has an interest in greener and sustainable sources for the production of goods

and services. The IC₅₀ values of *C. longa* and standard are shown in Table 2 and the % DPPH radical-scavenging according to the volume of *C. longa* is shown in Figure 1.

3.3 Antimicrobial assessment by microdilution and disc diffusion method

The broth microdilution plates were prepared and read with a microplate reader at a wavelength of 630nm, it was observed in comparison with the 0.5 standard bacterial McFarland solution which has a standard turbidity measurement. Observably as the concentration of the treatment reduced, turbidity reduced likewise across test organisms. The MIC for this research was determined as the lowest concentration that didn't have color change after inoculating the microorganism with a similar concentration as the McFarland standard. In Table 3, the minimum inhibitory concentrations (MIC) and Minimum bactericidal concentration for *S. aureus* were 12.5 mg/ml and 25 mg/ml respectively. Figure 2 shows the MIC and MBC of *C. longa* on *S. aureus*.

The comparison of zone diameters at the disc diffusion test showed that there is a significant difference between the *Curcuma longa* extract compared with antibiotics and negative control ($p < 0.05$). Chloramphenicol used as a positive control was found to be most effective on *S. aureus*. However, *C. longa* methanol extract and penicillin G were found to have the same microbial inhibition due to the negative control by the Duncan test (Table 4).

Discussion

Many researchers who tested different plant extracts against bacteria and yeast observed their antimicrobial activities. Plant extracts contain lots of active chemical compounds which show potential antimicrobial activities. Plants whose have especially rhizomes contain lots of active substances in terms of antimicrobial and anticancer activities. *Curcuma longa* is one of these plants who has economic and industrially-important substances inside.

It was gathered by the observation that the qualitative extraction of *C. longa* using methanol shows the presence of varying chemical components such as AR-tumerone, arachinsaeure, alpha-tumerone amongst others (Table 1). Arachinsaeure finds its relevance in ointment formulation of face, body, and hand skincare products, moisturizers, anti-aging formulations, and other skincare products. Research data suggest that ar-turmerone has the potential to promote the positive and negative proliferation of tumor cell lines. However, ar-turmerone inhibited the proliferation of certain cancer cell lines, it enhanced the proliferation of a special type cell; peripheral blood mononuclear cells (14). Alternative research was conducted, showed that when the alpha tumerones and aromatic tumerones were used in the same amounts, a significantly higher amount of curcumin was detected inside the cells. The results also describe that changes in transport of curcumin are largely depended on the tumerones (15). Results showed that alpha tumerones mainly contributed to the

Table 1. Showing the GC-MS profiling of *Curcuma longa* methanol extract

S/N	Chemical compound name	Retention times (Mins)	Molecular formula
1	4-hydroxy-3-(2-oxo-2h-1-oxa-3-phenanthryl)-2(1h)-quinolone	5.583	C ₁₀ H ₇ NO ₄
2	1,2,2-Trimethylcyclopropylamine	7.717	C ₆ H ₁₃ N
3	Glycine, N-[[[(4-methoxyphenyl)methoxy]carbonyl]-N-methyl-	8.717	C ₂₅ H ₂₃ NO ₆
4	1,E-11,Z-13-Octadecatriene	15,517	C ₁₈ H ₃₂
5	13-Heptadecyn-1-ol (CAS) 1-HYDROXY HEPTADEC-13-YNE	15.942	C ₁₇ H ₃₂ O
6	Oleoylcholesterol	16,267	C ₄₅ H ₇₈ O ₂
7	1H-Purin-6-amine, [(2-fluorophenyl)methyl]-	16,775	C ₁₂ H ₁₀ FN ₅
8	AR-TUMERONE	18092	C ₁₅ H ₂₀ O
9	ALPHA.-TUMERONE	18642	C ₁₅ H ₂₂ O
10	6,9,12-Octadecatrienoic acid, phenyl methyl ester	23933	C ₁₉ H ₃₂ O ₂
11	ARACHINSAEURE	24383	C ₂₀ H ₄₀ O ₂

Table 2. *Curcuma longa* extracts and standards showing IC50 values

Samples analyzed	IC50 values
<i>Curcuma longa</i> methanol extract	3.2 mg/ml
Ascorbic acid standard	5 mg/ml

Figure 1. % DPPH radical-scavenging according to the volume of *C. longa***Table 3.** Showing the minimum inhibitory concentrations (MIC) and minimum bactericidal concentration (MBC) for *Staphylococcus aureus*

Microorganisms	<i>Staphylococcus aureus</i> (B-4420)			
Concentration (mg/ml)	50	25	12.5	6.25
Methanol turmeric extract	-	-	+	+

Figure 2. Mueller Hinton microplates showing MIC and MBC of *Curcuma longa* on *Staphylococcus aureus*

Table 4. Showing the zone of inhibition for *Staphylococcus aureus* by Duncan test

Duncan ^a CONS	N	Subset for alpha = .05		
		1	2	3
N (Dimethyl Sulfoxide)	6	5,02		
<i>Curcuma longa</i> methanol extract	6		8,07	
PEN (Penicillin G)	6		8,21	
CHL (Chloramphenicol)	6			12,83
Sig.		1,000	,791	1,000

Means for each tested samples in homogeneous subsets are displayed.

^a. Uses Harmonic Mean Sample Size = 6,000.

changes in curcumin transport across and into the Caco-2 cells. Actually, in the presence of alpha, the measured curcumin amounts inside the cells and on the basolateral side of the monolayer were significantly increased which is one of the compounds responsible for antimicrobial activity according to (6). In addition, the solvent of extraction plays a role in adequate phenotyping and phytochemical examination in the GC-MS. Czernicka et al. (16) detected different substances in *C. longa* according to ours by LC-MS analysis as a result of methanol and diethyl ether extract. Kukula-Koch et al. (17) obtained many substances from *C. longa* with special solvent composed of heptane: chloroform: methanol: water mixture. Some of these items were similar to those in our study, while others differed. These researches show that lots of solvents can be used for extraction and different substance can be obtained if different analysis method and solvent are used. This situation might be as a result of the solvent of extraction which might interfere and alter the resultant constituents within the solvent (18).

This bottleneck is the rationale behind the focus of scientist on alternative orthodox or traditional means of sorting out human health problems by diet. Biomolecules have the ability.

Ascorbic acid was weighed and dissolved in both methanol. These methods were carried out to evaluate the antioxidant potential of *C. longa* methanol extracts and the interactions with free radicals. In vitro antioxidant assays have the potential to give a certain level of information that could contribute and give insight as to what happens in in vivo assay. Ascorbic acid has very high standard antioxidant activity, the percentage of DPPH scavenging activity appeared to increase as concentration increased for both the standard and the *C. longa* methanol extracts (Figure 1). The absorbance appeared to be unstable at some concentrations and it was in opposition with what Zhang et al. (9) reported in similar research. Compared to the IC₅₀ values of Ascorbic acid which was 5 mg/ml, *C. longa* methanol extract had a lower IC₅₀ value is 3.2 mg/ml which according to previous literature is a good one given that lower IC₅₀ values indicate great antioxidant activity (Table 2).

The zones of inhibition were measured after plating on a Mueller-Hinton agar plate and compared to the standards penicillin G and chloramphenicol. The methanol extract of *C. longa* has antimicrobial effect against *S. aureus* known as infectious disease agent as well as tested antibiotics (Table 4). The literature explains that a wider zone of inhibition describes the increased antimicrobial activity of certain agents over others. The research reported by Akter et al. (8) showed that *C. longa* methanol extract was effective on *S. aureus* and it could be as a result of a larger surface area on smaller sized turmeric components which makes it easier to access the interior cell wall compartment of these microbes. Differences in the susceptibility of *S. aureus* might be due to the variances in the cell wall structure, physiology and metabolism (4). Jalaluddin et al. (19) found that *C. longa* extract was effective on some periodontal pathogens; *Porphyromonas gingivalis*, *Prevotella intermedia* and *Aggregatibacter actinomycetemcomitans*. This indicates that there is at least one substance in *C. longa* that has antimicrobial effects on many bacterial species. In our study, the dominant inhibition of *C. longa* extract on a species that is resistant to Methicillin proves that the turmeric plant has a high antimicrobial effect.

Conclusion

Curcumin has shown potent antioxidant, anticancer, antibacterial, antifungal activity and other pharmacological actions since 1950. Nowadays, Curcumin has been sold globally as a food and health supplement mainly for its anti-inflammatory and antioxidant properties. However, the GC-MS typing did not identify this curcumin, moreover research suggests that active agent for antimicrobial activity is curcumin. This indicates that different components other than curcumin, which are contained in *C. longa*, have an antimicrobial effect. *C. longa* methanol extract had a lower IC₅₀ value with 3.2 mg/ml which according to previous literature is a good one given that lower IC₅₀ values indicate great antioxidant activity. This result showed that *C. longa* methanol extract was effective on Methicillin-resistant *S. aureus* and it could be a potential antimicrobial agent with its contents against *S. aureus*.

It has high potential to be developed into an antibiotic against Methicillin-resistant *Staphylococcus aureus* and other clinically important bacterial strains in future. However, in order to develop biologically more active curcumin and other substance derivatives available in *C. longa*, it is necessary to increase the number of studies and to test its effectiveness in situ and in vitro conditions by switching to the production of new generation synthetic products.

References

- Angel GR, Menon N, Vimalaa B, Nambisan B. Essential oil composition of eight starchy *Curcuma* species. *Ind Crops and Prod* 2014; 60:233-238. doi: 10.1016/j.indcrop.2014.06.028.
- Ilangovan M, Gunaab V, Hucde C, Naganandaa GS, Reddy N. *Curcuma longa* L. plant residue as a source for natural cellulose fibers with antimicrobial activity. *Ind Crops and Prod* 2018; 112: 556-560. doi: 10.1016/j.indcrop.2017.12.042.
- Kutti Gounder D, Lingamallu J. Comparison of chemical composition and antioxidant potential of volatile oil from fresh, dried and cured turmeric (*Curcuma longa*) rhizomes. *Ind Crops and Prod* 2012; 38(1): 124-131. doi: 10.1016/j.indcrop.2012.01.014.
- Rahman AFMM, Angawi RF, Kadi AA. Spatial localisation of curcumin and rapid screening of the chemical compositions of turmeric rhizomes (*Curcuma longa* Linn.) using Direct Analysis in Real Time-Mass Spectrometry (DART-MS). *Food Chem* 2015; 173: 489-494. doi: 10.1016/j.foodchem.2014.10.049.
- Singh G, Kapoor IPS, Singh P, de Heluani CS, de Lampasona MP, Catalan CAN. Comparative study of chemical composition and antioxidant activity of fresh and dry rhizomes of turmeric (*Curcuma longa* Linn.). *Food Chem Toxicol* 2010; 48(4): 1026-1031. doi: 10.1016/j.fct.2010.01.015.
- Tavares WS, Freitas SS, Graziottini GH, Parente LML, Lião LM, Zanuncio JC. Ar-turmerone from *Curcuma longa* (Zingiberaceae) rhizomes and effects on *Sitophilus zeamais* (Coleoptera: Curculionidae) and *Spodoptera frugiperda* (Lepidoptera: Noctuidae). *Ind Crops and Prod* 2013; 46: 158-164. doi: 10.1016/j.indcrop.2013.01.023.
- Krishnakumar IM, Kumar D, Ninan E, Kuttan R, Malikakel BP. Enhanced absorption and pharmacokinetics of fresh turmeric (*Curcuma longa* L) derived curcuminoids in comparison with the standard curcumin from dried rhizomes. *J Funct Foods* 2015; 17: 55-65. doi: 10.1016/j.jff.2015.04.026.
- Akter J, Hossain MA, Takaraa K, Islam MZ, Hou D-X. Antioxidant activity of different species and varieties of turmeric (*Curcuma spp*): Isolation of active compounds. *Comp Biochem Physiol C Toxicol Pharmacol* 2019; 215: 9-17. doi: 10.1016/j.cbpc.2018.09.002.
- Zhang L, Yang Z, Wei J, Su P, Chen D, Pan W, Zhou W, Zhang K, Zheng X, Lin L, Tang J, Du Z. Contrastive analysis of chemical composition of essential oil from twelve *Curcuma* species distributed in China. *Ind Crops and Prod* 2017; 108: 17-25. doi: 10.1016/j.indcrop.2017.06.005.
- Vutakuri N. Curcumin - Breast Cancer Therapeutic Agent to Replace Allopathic Treatments with Extensive Side Effects. *J Young Investig* 2018; 35(2): 38-44. doi: 10.22186/jyi.35.2.38-44.
- Song X, Zhang M, Dai E, Luo Y. Molecular targets of curcumin in breast cancer (Review). *Mol Med Rep* 2019; 19(1): 23-29. doi: 10.3892/mmr.2018.9665.
- Perrone D, Ardito F, Giannatempo G, Dioguardi M, Troiano G, Russo LL, de Lillo A, Laino L, Muzio LL. Biological and therapeutic activities, and anticancer properties of curcumin (Review). *Exp Ther Med* 2015; 10(5): 1615-1623. doi: 10.3892/etm.2015.2749.
- Ukwubile CA, Ahmed A, Katsayal UA, Ya'u J, Mejida S. GC-MS analysis of bioactive compounds from *Melastomastrum capitatum* (Vahl) Fern. leaf methanol extract: An anticancer plant. *Scientific African* 2019; 3: 10-17. doi: 10.1016/j.sciaf.2019.e00059.
- Hucklenbroich J, Klein R, Neumaier B, Graf R, Fink GR, Schroeter M, Rueger MA. Aromatic-turmerone induces neural stem cell proliferation in vitro and in vivo. *Stem Cell Res Ther* 2014; 5(4): 1-9. doi: 10.1186/scrt500.
- Yue GGL, Cheng S-W, Yu H, Xu Z-S, Lee JKM, Hon P-M, Lee MYH, Kennelly EJ, Deng G, Yeung SK, Cassileth BR, Fung K-P, Leung P-C, Lau CBS. The role of turmerones on curcumin transportation and P-glycoprotein activities in intestinal caco-2 cells. *J Med Food* 2012; 15(3): 242-252. doi: 10.1089/jmf.2011.1845.
- Czernicka L, Grzegorzczak A, Marzec Z, Antosiewicz B, Malm A, Kukula-Koch W. Antimicrobial potential of single metabolites of *Curcuma longa* assessed in the total extract by thin-layer chromatography-based bioautography and image analysis. *Int J Mol Sci* 2019; 20(4): 898. doi: 10.3390/ijms20040898.
- Kukula-Koch W, Grabarska A, Łuszczki J, Czernicka L, Nowosadzka E, Gumbarewicz E, Jarzab A, Audo G, Upadhyay S, Głowniak K, Stepulak A. Superior anticancer activity is demonstrated by the total extract of *Curcuma*

- longa* L. as opposed to individual curcuminoids separated by centrifugal partition chromatography. *Phytother Res* 2018; 32(5): 933-942. doi: 10.1002/ptr.6035
18. Teow SY, Liew K, Ali SA, Khoo ASB, Peh SC. Antibacterial Action of Curcumin against *Staphylococcus aureus*: A Brief Review. *J Trop Med* 2016; 2016: 2853045. doi: 10.1155/2016/2853045.
 19. Jalaluddin M, Jayanti I, Gowdar IM, Roshan R, Varkey RR, Thirutheri A. Antimicrobial Activity of *Curcuma longa* L. Extract on Periodontal Pathogens. *J Pharm Bioallied Sci* 2019; 11(2): 203-207.