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Curcumin (*Curcuma Longa*) and Quercetin Nanoparticles as Anticancer Agents for HepG2 and HCT116 Human Cell Lines

Soheir N. Abd El-Rahman*and Raafat N. Sandak

Crops Technology Research Department, Food Technology Research Institute, Agricultural Research Center, Giza, Egypt

Abstract

Curcumin and quercetin are very poor water solubility, it could be these bio products useful and important in condition therapy related with cancer, oxidative stress and can used it to develop functional foods and to improve the foods shelf life. The objective was to prepare Curcumin and quercetin nanoparticles (CurNPs and QurNPs) give highly stable and soluble in water. The DPPH radical scavenging activity, HepG2 and HCT116 human cell lines (human cancer liver and colon) and antimicrobial of CurNPs and QurNPs were determined. The results showed that the CurNPs and QurNPs had the highest DPPH free radical scavenging activity at concentrate 1000 µg/ml were 94.91 and 98.11%, these results equal or nearly from ascorbic acid as at positive control at the same concentrate was 98.69%. CurNPs and QurNPs were significantly increased cell cytotoxicity, from the minimum to maximum concentrations ranging from 6.25 to100 µg/ml in HepG2 human cell lines (human cancer liver) which inhibition these cells at concentrate 100 µg/ml were 87.434 and 87.848% and the viability cells were 12.566 and 12.152%, IC_{50} = 31.15, 5.80, respectively. Meanwhile, the HCT116 human cell lines (human cancer colon), results found that the inhibition cells were 93.112 and 92.893% and the viability cells were 7.888, 7.1075 and IC_{50} = 22.65, 6.68, respectively. The highest inhibition zone in gram-positive bacteria than gram-negative bacteria was at 100µg/ml. Therefore, it could be recommended that drugs within nanoparticles enhance the entry of drugs within tumor tissues in vivo and antimicrobial by the enhanced retention and permeation effect.

Keywords: Curcumin nanoparticles • Quercetin nanoparticles • HepG2 • HCT116 • DPPH • Antimicrobial

Introduction

Curcumin has been widely used as a therapeutic potential as an anti-inflammatory, anti-oxidant and anti-cancer agent [1], antiaging, lowering diabetes, anti-microorganisms, anti-vascular diseases, and anti-blood pressure [2]. Curcumin prevents lipid peroxidation and maintains the level concentration of intracellular antioxidant enzymes, and scavenges free reactive species effectively [3]. These nutritional characteristics of curcumin are likely to be referred to the methoxy, hydroxyl, α, an unsaturated carbonyl group [4].

Colorectal cancer is the third most common type of cancer diagnosed globally. Clinically, chemotherapeutic agents are the mainstay of treating colorectal cancer. However, the side effects of chemotherapeutics encourage advancing adjuvants, which exhibit the best safety, such as turmeric extract (TE), which has been an inhibitory influence on colon cancer [5].

Curcumin inhibited colon cancer being developed by preventing cell proliferation and cell survival, improving cell uptake, activating the caspases cascade, demonstrating controlled release at physiological pH, and enhancing endogenous apoptotic signaling [6]. The results were revealed that curcumin inhibited the viability of Huh-7, MHCC-97H, and HepG2 cells and the growth of HepG2 xenograft tumors in rats [7].

Li et al. [8] showed that curcumin suppressed HCC growth in vivo and prevented HCC cell proliferation and caused cell apoptosis. MiR-21 inhibition increased the influence of curcumin on cell proliferation prevention, apoptosis, and TGF-β1/smad3 signaling by prevention in HepG2 and HCCLM3 cells.

Quercetin (3,3,4,5,7-pentahydroxy flavone) (QUE), soluble in the fat compounds. It decreases fat hydro-peroxide production and is also able to inhibit fat damage, inhibits bio-molecular oxidation and radical scavenging, and alters antioxidant defense by in vivo and in vitro [9]. QUE is a flavonoid found in many foods and is known to be current in elevated ratios in onions, apples, broccoli, and green tea [10]. Numerous researches has concentrated on the beneficial characteristics of QUE, as anti-production, anti-microorganisms, anti-inflammatory, anti-cancer, and anti-aging influences, encouragement of antioxidant enzymes in the human body [11].

In addition, QUE is a difficult molecule that may be caused to its poor water solubility. It was synthesized but its bioavailability was only 20% [12]. and it has weak absorption in the gastrointestinal tract. All this highlights the necessity for became better formulation preparing QUE with improved solubility, and therefore, its absorption can be significantly important. Thus, Micro- and nanoparticle are being the most of great significance approaches which studied these days to become better bioavailability [13]. Nanoparticles are beneficial in drugs to help for water-insoluble compounds like ellagic acid and coenzyme Q10 may be due to elevating the absorption and the bioavailability of the delivered drug. NPS with various starting amounts of quercetin were utilized to estimate how the amount of quercetin influences the characteristics of nanoparticles and anti-microorganism efficacy [14,15].

Therefore, this study aimed to assess the antioxidant activity potential (DPPH) of CurNPs and QurNPs, also, its effect in the prevention and tries the treatment cancer Hepatocellular and colon; in addition, their effect on gram-positive and negative bacteria.

Materials and Methods

Materials

Quercetin and curcumin were purchased from Sigma-Aldrich, Singapore, and used as received. All reagents used were of technical grade. The absolute ethanol (99.5-99.8%) was obtained from J.T. Baker (Avantor Performance materials, Phillipsburg, NJ). Poly (D,L-lactic-co-glycolic acid) (PLGA) (Resomer R503H; MW 35-40 kDa), poly (vinyl alcohol) (PVA) (MW 30–70 kDa).

HCT-116 cells (human colon cancer cell line), and HepG-2 cells (human Hepatocellular carcinoma) obtained from VACSERA Tissue Culture Unit. 1, 1- diphenyl-2-picrylhydrazyl radical (DPPH), was purchased from Sigma-Aldrich (St. Louis, MO, USA). L-ascorbic acid was purchased from Merck Co.

***Address for Correspondence:** Abd El-Rahman SN, Crops Technology Research Department, Food Technology Research Institute, Agricultural Research Center, Giza, Egypt. E-mail: soheirkenawy@yahoo.com/ raafatsandak@gmail.com*

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(Darmstadt, Germany). All of the chemicals and reagents used in this study were of analytical grade.

Methods

Preparation of quercetin nanoparticles (QUNPs)

Quercetin was prepared by adding ethanol 70%, under magnetic stirring (1000 rpm) according to the nano participation technique according to Kakran et al. [16] and Abd El-Rahman and Al-Jameel [17].

Preparation of Curcumin nanoparticles (CurNPs)

Nanoparticles loaded with curcumin were prepared by a modified emulsion diffusion evaporation method according to Devadasu et al. [18]. Curcumin (7.5 mg) and Poly (lactide -co- glycolide) acid (PLGA) (50 mg) were dissolved in 2.5 ml of ethyl was continued for 5 min at 15,000 rpm. The supernatant was separated and the pellet was redispersed in 20 ml water, then the curcumin nanoparticles with *Polyvinyl alcohol* (*PVA*) (50 mg), used as a stabilizer, were dissolved in 5 ml distilled water.

Determination of antioxidant activity (Scavenging Activity of DPPH Radical)

The DPPH free radical scavenging of CurNPs and QurNPs was measured according to Emile et al. [19]. Different concentrations of CurNPs and QurNPs (10, 50, 100, 500, and 1000 µg /ml) were compared with ascorbic acid. The decrease in absorbance was measured at λ= 517 nm.

Mammalian cell lines

Potential Mammalian cell lines: HCT-116 cells (human colon cancer cell line), and HepG-2 cells (human Hepatocellular carcinoma) were tested using the method of Gomha et al., [20].

Antimicrobial activity

The antimicrobial activity of samples was determined using the method Scott [21] CurNPs and QurNPs size were tested against Gram-positive bacteria like *Streptococcus aureus, Streptococcus penoenumoia* and *Bacillus substilis*, in addition, Gram-negative bacteria as *Escherichia coli, Salmonella typhimrium* and *Pseudomonas aeruginosa*.

CurNPs and QurNPs size were dissolved in a 70% ethanol solution of in a final concentration of f10 mg/mL. In addition, the CurNPs and QurNPs size solvent was assayed at concentrations of 25, 50, 75, and, 100 µg/L.

Method of testing

The sterilized media were poured onto the sterilized Petri dishes and wells of 6 mm diameter were made in the Petri dishes medium. A sterile swab was used to evenly distribute microbial suspension over the surface of solidified media and the different concentrations were added to each well using a micropipette and incubated at 37°C for 24 hrs. moreover, the zones of inhibition were measured on an mm. Scale.

Statistical analysis

Statistical analysis Means ± SD of the results are analyzed utilizing one-way analysis of difference (ANOVA), which was used for all statistical analyses according to Silva and Azevedo [22].

Results and Discussion

Effect of CurNPs and QurNPs on DPPH scavenging activity

Definition of antioxidant is the efficiency to neutralize free radicals that are generated in increase caused to environmental effects. The body's defense mechanisms usually demand support in inhibiting the influences of oxidative stress [23].

The effects antioxidant activity as DPPH on CurNPs and QurNPs and compared with ascorbic acid which has been at different concentrations were measured and the results are shown in Table 1. The results observed that the highest concentration from CurNPs and QurNPs had the highest DPPH free radical scavenging activity at concentrate 1000 µg/ml were 94.91 and 98.11%, these results equal or nearly from ascorbic acid as at positive control at the same concentrate was 98.69%.

Curcuminoid is a compound in natural antioxidants that scavenging free radicals [24]. The antioxidative activity of Curcumin compounds is 20, 9, and 8 times higher compared with α-tocopherol [25].

Quercetin (C15H10O7), 3, 3', 4', 5, 7-pentahydroxyflavone, is one of the flavonoids, which has been widely utilized for its antioxidant, anti-inflammatory, and anti-cancer characteristics [26]. Prevention of radical action and chelating characteristics was enhanced when quercetin and catechin nanoparticles [27].

CurNPs and QurNPsonliver cancer human cell lines

Effect of CurNPs and QurNPs extract and compared with Wish Cells (Human normal cells) on different concentrations were determined on Hepatocellular Carcinoma (HCC) (HEPG-2 Cells) and the results are shown in Table 2. From the results, it could be noticed that the effect of Wish Cells (Human normal cells) on the HEPG-2 Cells at concentrate 100 µg/ ml, viability HEPG-2 Cells was the lowest (3.275%), which means the highest inhibition ratio was 96.725%. Whilst, the results from CurNPs and QurNPs sizes extract at the same concentration the viability HEPG-2 Cells was 12.566, 12.152% and IC_{50} = 31.15, 5.80, respectively, to give the same inhibition ratio to HEPG-2 Cells. Furthermore, the results observed that at a high concentration of CurNPs and QurNPs extract to award the greatest response the size of CurNPs and QurNPs extract may be caused as natural antioxidant compounds against cancer.

Other concentrations for CurNPs and QurNPs at 6.25, 12.5, 25.0, and 50.0 µg/ ml, the results were observed that viability HEPG-2 Cells for CurNPs were 88.262, 72.498, 51.279, and 48.044%, as well as, viability HEPG-2 Cells for QurNPs were 44.338, 43.681, 38.807 and 37.509%, respectively. Recent studies have demonstrated that curcumin has anticancer characteristics in different cancer cell models and objects a variety of biological by included in cell cycle regulation, apoptosis, mutagenesis, angiogenesis, and metastasis [28].

Curcumin has shown powerful antitumor activities with low cytotoxicity to normal cells [29]. Curcumin has been observed to prevent the spread of different kinds of cancer, including Hepatocellular Carcinoma (HCC). Curcumin exerts potent anticancer characteristics by regulating a series of signaling pathways and molecular objects [30]. Although more mechanisms have been suggested regarding curcumin as an against HCC agent, the exact mechanism of curcumin is not fully understood.

Quercetin is a flavonoid with beneficial influences in numerous human troubles, including liver cancer. More studies confirmed that quercetin is a promising antitumor agent, not only as a single therapy but also beneficent current therapeutic options against advanced HCC [31].

From the IC_{50} results, it could be found that the CurNPs and QurNPs preserved the anticancer activity of liver cancer cell lines.

CurNPs and QurNPson colon cancer human cell lines

The cytotoxicity of CurNPs and QurNPs was tested on colon cancer HCT 116 cell lines at concentrations from zero to 100 µg/ ml and the results are reported in Table 3.

From the results, it could be noticed that the effect of QurNPs on colon cancer HCT 116 cell lines gives the best results viability during the gradually concentrations 6.25, 12.5, 25.0, 50.0 and 100.0 µg/ ml, the viability was 46.857, 41.253, 39.555, 35.689 and 7.107%, respectively. The nanoparticles used as carriers for the delivery of quercetin into target cells have been evaluated in different diseases [32]. On the one hand, nanoparticles alone offer a system that causes damage to specific cells by mechanisms such as oxidative stress, lipids and proteins oxidation, and high toxicity due to their physicochemical

Table 1: DPPH scavenging activity forCurNPs and QurNPs.

Concentration µg/ml	Scavenging activity %		
	CurNPs	QurNPs	Ascorbic acid (positive control)
10	9.23	62.47	47.72
50	20.60	91.16	92.63
100	42.42	95.90	95.81
500	92.82	96.29	97.91
1000	94.91	98.11	98.69

Table 2: Effect of CurNPs and QurNPs on Viability of HEPG-2 Cells (Liver Cancer).

Concentration µg/ ml	CurNPs	QurNPs	Wish Cells (Human normal cells)
0	100	100	100
6.25	88.2619	44.3379	80.3506
12.5	72.4981	43.6795	68.5417
25	51.2792	38.8073	58.7748
50	48.0436	37.5094	37.9503
100	12.5658	12.1520	3.2749
IC_{50}	31.15	5.80	26.66

Table 3: Effect of CurNPs and QurNPs on Viability of HCT116 Cells (Colon Cancer).

Concentration µg/ ml	CurNPs	QurNPs	Wish Cells (Human normal cells)
0	100	100	100
6.25	85.553	46.857	66.4309
12.5	59.001	41.253	58.8761
25	45.373	39.555	54.8009
50	40.843	35.689	48.7719
100	7.888	7.107	45.8318
IC_{50}	22.65	6.68	4.68

characteristic as the superficial charge [33]. In some cases, like cancer, central nervous degeneration, and cardiovascular diseases damage is generated by oxidative stress [34].

Li *et al.* [35] emphasized the powers of quercetin to inhibit cancer advancement by impeding the inflammation-producing enzymes and decreasing the production of pro-inflammatory mediators. Therefore, it plays become better role in immunity and fungal infections and is gradually considered an important factor in several stages of cancer development [36].

Whilst, the effect of CurNPs colon cancer HCT 116 cell lines at the same concentrations found that the viability was 85.553, 59.001, 45.373, 40.843, 7.888%, respectively. Curcumin nanoparticles were examined for their anticancer activity on colon cancer HCT-116 lines, lung cancer cell line A549, and prostate cancer cell line PC3. The safety of the preparation was tested on the fibroblasts' cell lines. The results demonstrated that curcumin nanoparticles proved to be safe on the normal fibroblast cell lines, and maintained anticancer activity against A549, HCT116, and PC3 cell lineages [37].

CurNPs and QurNPs as antimicrobial agent

Antibacterial activity was studied with the ethanol extract from CurNPs at different concentrations 25, 50, 75, and100 µg/ml were determine the zone of inhibition of gram-positive and gram-negative bacterial growth, and the results are reported in Table 4.

The results in Table 4 indicated that the CurNPs extract was gradually inhibiting zone from concentration 25µg to 100µg in gram-positive and gram-negative. In addition, the highest inhibition zone at 100 µg concentration in gram-positive bacteria was *Bacillus subtitles, Streptococcus penoenumoia*. *And Streptococcus aureus* was 70.8, 42.3 and 40.5 mm respectively. Whilst, in gram-negative bacteria the highest inhibition zone at 100 µg concentration for *Escherichia coli* and *Salmonella typhimrium* was 50.5 and 35.7 mm, and also the CurNPs extract at 100 µg had not been detected on *Salmonella typhimrium*. Singh et al. [38] found that the nano-curcumin is freely dispersible in water and this dispersion of nano-curcumin was more effective than curcumin against gram-positive and negative bacteria. The results showed that the antimicrobial activity of curcumin nanoparticles has significantly become better. Furthermore, the activity of nano-curcumin was more pronounced against Gram-positive bacteria than Gram-negative bacteria. The mechanism of the antibacterial influence of curcumin nanoparticles was observed that these particles entered the inside of the bacterial cell by completely breaking the cell wall, which led to cell death.

The mechanism of the antibacterial activity of curcumin seems to differ depending on the strain. Therefore, the CurNPs showed that stronger antibacterial activity against *Escherichia coli* [39].

The result in Table 5 shows the effect of QurNPs as an antimicrobial agent (gram- positive and gram-negative bacteria). The results observed that the highest inhibition zone in gram-positive bacteria was *Bacillus subtitles, Streptococcus penoenumoia and Streptococcus aureus,* at concentrate 100µg were 62.5, 47.4, and 45.3 mm, respectively. Meanwhile, in gram-negative bacteria the highest inhibition zone at concentrate 100µg was *Escherichia coli* and *Salmonella Typhimrium* by 60.2 and 40.8 mm, respectively, and also the QurNPs extract at 25, 50 and 75 µg had not been detected on *Salmonella typhimrium* at 100µg.

The results confirmed that the antimicrobial activity of both quercetin NPs and free quercetin was effective on gram-positive strains [14].

Conclusion

Curcumin and quercetin nanoparticles had the highest contained antioxidant activity. Therefore, it exhibits anticancer influence against HepG2 and HCT116 human cell lines (human cancer liver and colon) in addition to antimicrobial gram-positive and gram-negative bacteria. Thus, the role of Curcumin and quercetin nanoparticles in health status may be due to bioactive compounds as natural antioxidants. Therefore, nutritional factors to be taken

Table 4: CurNPs as antimicrobial agent.

	Concentration (µL)			
	25	50	75	100
***Gram-positive* (mm)**				
Streptococcus aures	4.2±0.02	10.4±0.82	20.3±1.25	40.5±3.18
Streptococcus penoenumoia	10.5±0.31	15.4±0.97	29.6.3±1.31	42.±3.73
Bacillus subtitles	11.9±0.74	20.5±1.83	40.41±2.57	70.8±5.11
***Gram-negative*(mm)**				
Pseudomonasaeruginous	ND	ND	ND	ND
E. coli	9.5±0.251	14.7±0.94	32.8.6±2.36	50.4±3.24
Salmonella typhimrium	6.3±0.83	12.7±0.98	20.6±1.73	35.7.1±2.46

Values are mean and SD (n = 3) ND = not detect

Table 5: QurNPs as antimicrobial agent.

	Concentration (µL)			
	25	50	75	100
***Gram-positive* (mm)**				
Streptococcus aures	7.5±0.38	9.5±0.48	18.3±0.99	45.3±3.55
Streptococcus penoenumoia	11.6±0.57	17.5±0.95	32.5±2.72	47.4.7±3.19
Bacillus subtitles	12.9±0.66	25.28±1.22	48.3±3.33	62.5±5.29
***Gram-negative*(mm)**				
Pseudomonasaeruginous	ND	ND	ND	ND
E. coli	13.9±0.54	23.6±1.09	47.5±3.37	60.2.3±5.86
Salmonella typhimrium	12.4±0.64	17.5±0.87	22.1±1.07	40.28.0±3.94

Values are mean and SD (n = 3) ND = not detect

very seriously by increased care as a preventative and lower considerable side effect of cancer chemical drugs.

References

1. Kunnumakkara, AB., Anand P and Aggarwal BB. "Curcumin inhibits proliferation, invasion, angiogenesis and metastasis of different cancers through interaction with multiple cell signaling proteins". *Cancer Lett* 2008; 269: 199-225.
2. Rainey N. "Curcumin hormesis mediates a cross-talk between autophagy and cell death". *Cell Death Dis* 2015; 6: e2003-e2011.
3. Suryanarayana, P., Satyanarayana A, Balakrishna N, Kumar PU and Reddy GB. "Effect of turmeric and curcumin on oxidative stress and antioxidant enzymes in streptozotocin-induced diabetic rat". *Med Sci Monit* 2007; 13: 286-292.
4. Aggarwal, BB., Gupta SC, and Sung B. "Curcumin: an orally bioavailable blocker of TNF and other pro-inflammatory biomarkers". *Br J Pharmacol* 2013; 169(8): 1672-1692.
5. Li, M., Yue GGL, Luo L, Tsui SKW, and Fung KP, et al. "Turmeric Is Therapeutic in Vivo on Patient-Derived Colorectal Cancer Xenografts: Inhibition of Growth, Metastasis, and Tumor Recurrence". *Front Oncol* 2021; 10(574827): 1-16.
6. Waghela BN. "Curcumin conjugated with PLGA potentiates sustainability, anti-proliferative activity and apoptosis in human colon carcinoma cells". *PLoS One* 2015; 10(2): e0117526.
7. Tian, S., Liao L, Zhou Q, Huang X, and ZhenG P, et al. "Curcumin inhibits the growth of liver cancer by impairing myeloid-derived suppressor cells in murine tumor tissues". *Oncol Letters* 2021; 21: (286): 1-10.
8. Liu, H., Han Y, Wang T, Zhang H, and Xu Q, et al. "Targeting Microglia for Therapy of Parkinson's Disease by Using Biomimetic Ultra small Nanoparticles". *J Am Chem Soc*. 2020; 142: 21730-21742.
9. Cione, E., La Torre C, Cannataro R, Caroleo MC, and Plastina P, et al. "Quercetin, Epigallocatechin Gallate, Curcumin, and Resveratrol: From Dietary Sources to Human MicroRNA Modulation". *Molecules* 2019; 25: 63.
10. Nathiya, S., Durga M, and Thiyagarajan D. "Quercetin, encapsulated quercetin and its application-a review". *Int J Pharm Sci* 2014; 10: 20-26.
11. Khan, F., Niaz K, and Maqbool F. "Fatima Ismail Hassan; Mohammad Abdollahi; Kalyan C. Nagulapalli Venkata; Seyed Mohammad Nabavi; Anupam Bishayee; Molecular Targets Underlying the Anticancer Effects of Quercetin: An Update. Nutrients". 2018; 8 (529): 10.
12. Acevedo-Fani, A., Soliva-Fortuny R, and Martín-Belloso O. "Nanostructured emulsions and nanolaminates for delivery of active ingredients: Improving food safety and functionality". *Trends Food Sci Technol* 2017; 60: 12-22.
13. Faridi Esfanjani, A., and Jafari SM. "Biopolymer nano-particles and natural nano-carriers for nano-encapsulation of phenolic compounds". *Colloids Surf. B Biointerfa* 2016; 146: 532-543.
14. Arasoğlu, T., Derman S, Mansuroğlu B, Uzunoğlu D, Koçyiğit B, and Gümüş B et al. "Preparation, characterization, and enhanced antimicrobial activity: quercetin-loaded PLGA nanoparticles against foodborne pathogens". *Turk J Biol* 2017; 41: 127-140.
15. Basak, P., Adhikary T, Das P, and Biswas S. "Phytochemical analysis and comparative study of antibacterial effect of turmeric extracts using different solvent". *IOP Conf. Series: Mat Sci and Eng* 2018; 410: 1-8.
16. Kakran, M., Ahoo S, NG Li, and Judeh Z. "Fabrication of quercetin nanoparticles by anti-solvent precipitation method for enhanced dissolution". *Powder Technology* 2012; 223: 59-64.
17. El-Rahman, Abd., S. N, and Al-Jameel SS. "Quercetin Nanoparticles: Preparation and Characterization". *Int J of Drugs* 2014; 2(3): 96-103.
18. Devadasu, VR., Wadsworth RM, and Ravi Kumar MNV. "Protective Effects of Nano particulate Coenzyme Q10 and Curcumin on Inflammatory Markers and Lipid Metabolism in Streptozotocin-induced Diabetic Rats: A Possible Remedy to Diabetic Complications", Drug Delivery and Trans Res 2011; 1: 448-455.

19. Emile, C., Bazile D, Herman F, Helene C, and Veillard M. *Drug Deliv* 1996; 3: 187-190.

20. Gomha, SM., Riyadh SM, Mahmmoud EA, and Elaasser MM. "Synthesis and Anticancer Activities of Thiazoles, 1, 3-Thiazines, and Thiazolidine Using Chitosan-Grafted-Poly (Vinyl pyridine) as Basic Catalyst". *Heterocycles* 2015; 91: 1227-1243.

21. Scott AC. "Laboratory control of antimicrobial therapy. In: Collee JG *et al*. eds. *Practical Medical Microbiology*, 13th edn. Edinburgh: Churchill Livingstone". 1989: 161-181.

22. Silva, FA., and Azevedo CA. "Principal Components Analysis in the Software assist at Statistical Assistance". 7th World Congress on Computers in Agriculture Conference Proceedings, Reno. June 2009.

23. Jakubczyk, K., Druźga A, Katarzyna J, and Skonieczna-Żydecka K. "Antioxidant Potential of Curcumin—A Meta-Analysisof Randomized Clinical Trials, Antioxidants". 2020; 9 (1092): 1-13.

24. Achmad, SA., Hakim EU, Makmur L, Syah YM, Juliawaty LD, and Mujahidin D et al. "Ilmu kimia dan kegunaannya, tumbuh-tumbuhan obat Indonesia. Jilid I. Penerbit ITB, Bandung". 2007.

25. Widowati, W., Mozef T, Risdian C, Ratnawati, H, Tjahjani S, and Sandra F et al. "Inhibitor properties of *Piper betle* L., *Catharanthus roseus* [L] G.Don, *Dendrophtoe petandra* L., *Curcuma mangga* Val. Extracts on T47D cancer cell Line". *Int. Res. J. Biochem. Bioinform* 2011; 2(1): 22-28.

26. Bao, D., Wang J, Pang X, and Liu H. "Protective effect of quercetin against oxidative stress-induced cytotoxicity in rat pheochromocytoma (PC-12) cells". *Molecules* 2017; 22(7): 1-14.

27. Pool, H., Quintanar D, Figueroa JD, Camila J, Etelvino H, and Bechara LA et al. "Antioxidant Effects of Quercetin and Catechin Encapsulated into PLGA Nanoparticles". *J of Nanomat* 2012: 1-12.

28. Kunnumakkara, AB., Bordoloi D, Padmavathi G, Monisha J., Roy Nk, and Prasad S et al. "Curcumin, the golden nutraceutical: multitargeting for multiplechronic diseases". *Br J Pharmacol* 2016; 174: 1325-1348.

29. Aggarwal, BB., Yuan W, Li S, and Gupta SC. "Curcumin free turmeric exhibits anti-inflammatory and anticancer activities: identification of novel components of turmeric," *Molecular Nutrition & Food Research* 2013; 57(9): 1529-1542.

30. Zhang, L., Cheng X, and Gao Y. "Curcumin inhibits metastasis in human papillary thyroid carcinoma BCPAP cells via down-regulation of the TGF-*β*/ Smad2/3 signaling pathway," *Experimental Cell Research* 2016; 341(2): 157-165.

31. Wu, H., Pan L, Gao C, Xu H, Li Y, and Zhang L et al. "Quercetin Inhibits the Proliferation of Glycolysis-Addicted HCC Cells by Reducing Hexokinase 2 and Akt-mTOR Pathway". *Molecules* 2019; 24 (1993): 1-11.

32. Li, J., Wei H, Liu Y, Li Q, Guo H, and Guo Y et al. "Curcumin Inhibits Hepatocellular Carcinoma via RegulatingmiR-21/TIMP3 Axis, Evidence-Based Complementary and Alternative Medicine". 2020: 1-13.

33. Gurunathan, S., Jeyaraj M, Kang MH, and Kim JH. "Melatonin enhances palladium-nanoparticle-induced cytotoxicity and apoptosis in human lung epithelial adenocarcinoma cells a549 and h1229". *Antioxidants* 2020; 9: 1-29.

34. Fleming, E., and Luo Y. "Co-delivery of synergistic antioxidants from food sources for the prevention of oxidative stress". *J Agric FoodRes* 2021; 3: 100107.

35. Li, Y., Yao J, Han C, Yang J, Chaudhry MT, and Wang S, et al. "Quercetin, Inflammation and Immunity". *Nutrients* 2016; 8: 167.

36. Hoesel, BA., and Schmid J. "The complexity of NF-_B signaling in inflammation and cancer". *Mol. Cancer* 2013; 12: 86.

37. Nasr, M., Awadallah A, Al-Karaki R, Madanat F, Alsunna L, and Sami K, et al. "Exploring the unique anticancer properties of curcumin nanoparticles". *Clin Oncol & Res* 2019; 2(3): 1-5.

38. Singh, B., Basniwal RK, and Buttar HS. "Curcumin Nanoparticles: Preparation, Characterization, and Antimicrobial Study". *J Agric and Food Chem* 2011; 59(5): 2056-2061.

39. Bhakay, A., Rahman M, Dave RN, and Bilgili E. "Bioavailability Enhancement of Poorly Water-Soluble Drugs via Nanocomposites: Formulation–Processing Aspects and Challenges". *Pharmaceutics* 2018; 10 (86): 1-26.

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