

Antimicrobial Activity of Curcumin

Subjects: **Microbiology**

Contributor: Jeffersson Krishan Trigo-Gutierrez , Ewerton Garcia de Oliveira Mima , Yuliana Vega Chacón

Curcumin (CUR) is a natural substance extracted from turmeric that has antimicrobial properties. Due to its ability to absorb light in the blue spectrum, CUR is also used as a photosensitizer (PS) in antimicrobial Photodynamic Therapy (aPDT).

curcumin

drug delivery systems

antimicrobial agents

microbial drug resistance

viruses

bacteria

fungi

photochemotherapy

1. Introduction

The global changes arising from globalization and climate change have a profound impact on human health, including infectious diseases ^{[1][2]}. The increased mobility of people, urbanization, greenhouse-gas emissions, pollution, deforestation, global warming, loss of sea ice, sea-level rise, extreme weather events with droughts and flood, etc., have all contributed to affect the transmission, prevalence, and spread of existing infections, such as vector-borne diseases, and the emergence of new pathogens ^{[1][2]}. In some cases, these infections have resulted in epidemics such as dengue and pandemics such as COVID-19, which the world is currently facing ^[3].

Notwithstanding the existence of anti-infective medications, other current concerns are the drug resistance arising from the misuse of antimicrobial agents and the emergence of multidrug-resistant species ^[4]. These problems are a challenge for humanity, especially when considering that the development of new drugs demands time and money. Thus, the repurposing of existing medications and alternative therapies, such as natural substances, has been investigated ^{[5][6][7]}.

Curcumin (CUR) is a yellow dye (diferuloylmethane—a natural polyphenol) found in turmeric (*Curcuma longa*), which is a plant native to India and Southeast Asia. Beyond its culinary use as food flavoring and coloring, CUR also has a potential application in medicine due to its therapeutic properties, which include antioxidant, anticancer, anti-inflammatory, and antimicrobial effects ^[8]. CUR is not toxic and, according to the Food and Drug Administration, it is “Generally Recognized as Safe” ^[9]. The literature shows a plethora of studies reporting the biological and pharmacological features of CUR on health. Comprehensive reviews are available on the anticancer ^[10], anti-inflammatory ^[8], and antimicrobial ^[11] effects of CUR.

Nonetheless, CUR is not soluble in water, unstable in solutions, and shows low bioavailability, poor absorption, and rapid elimination from the body ^[11]. For these reasons, organic solvents such as ethanol, methanol, acetone, and dimethyl sulfoxide (DMSO) have been used to solubilize CUR ^[12]. These drawbacks hinder the in vivo use of CUR

as a therapeutic agent. Thus, some approaches have been used to overcome the problems of CUR, such as the use of adjuvants and drug delivery systems. Piperine, a substance derived from black pepper, and lecithin, a phospholipid, have been associated with CUR to improve its bioavailability by blocking the metabolism of CUR and enhancing its gastrointestinal absorption [11]. Additionally, drug delivery systems have been used to solubilize CUR and protect it from degradation until it reaches the target tissue, where CUR is sustainably released [13].

Nanotechnology has been a promising field in medicine (nanomedicine). Nanoscale structures show intrinsic physical and chemical properties, which have been exploited as diagnostic and therapeutic tools [13][14]. The present study reviews the drug delivery systems (DDS) used for CUR, aiming at its antimicrobial effect. Although comprehensive reviews about the antimicrobial effect of CUR (encapsulated or not) are found elsewhere [15][16][17][18], they describe only the antibacterial and antifungal activities of CUR in DDSs. Our review summarizes the DDSs used for CUR as an antiviral, antibacterial, and antifungal agent, encompassing different nanosystems (colloids and metals) and the relevant issues of antimicrobial resistance and the emergence of new pathogens.

2. Free CUR

The broad-spectrum activity of CUR as an antibacterial, antifungal, and antiviral agent was reviewed previously [15][16]. Thus, this section reviews recent studies not covered by these reviews about the antimicrobial activity of free (non-encapsulated) CUR (**Table 1**) before reporting the DDS used for CUR.

Table 1. In vitro and in vivo studies using free CUR and curcuminoids as antimicrobial.

Solvent	Microorganism	Culture	Antimicrobial Method	CUR Concentration	Light/Ultrasonic Parameters	Reference
DMSO (0.4%)	ZIKV >DGEV	Cell infection	IC ₅₀ >IC ₉₀	5.62–16.57 μM	-	[19]
N/R	HPVA Tulane V	Cell infection	Viral survival	0.015 mg/mL	-	[20]
N/R	KSPV	Infected cells	EC ₅₀	Up to 6.68 μM	-	[21]
Aqueous <i>Piper nigrum</i> seed extract	SARS-CoV-2	Cell infection	IC ₅₀ Plaque reduction	0.4 μg/mL	-	[22]
DMSO (<0.4%)	SARS-CoV-1	Cell infection	Inhibition of viral replication	20 μM	-	[23]

Solvent	Microorganism	Culture	Antimicrobial Method	CUR Concentration	Light/Ultrasonic Parameters	Reference
N/R	SARS-CoV	In vitro	Viral inhibition	23.5 μ M	-	[24]
N/R	SARS-CoV	In vitro	papain-like inhibition	5.7 μ M	-	[25]
DMSO (1 w/v)	<i>S. aureus</i> <i>E. coli</i>	Planktonic	Inhibition zone MIC	600 and 400 μ g/mL	-	[26]
DMSO	MRSA	Planktonic	MIC FICI	15.5 μ g/mL	-	[27]
N/R	<i>S. aureus</i> MSSA MRSA	Planktonic	Colony count	100 μ g/mL	8 or 20 J/cm ²	[28]
DMSO (10%)	<i>S. aureus</i>	Biofilm	aPDT	20, 40, and 80 μ M	5.28 J/cm ²	[29]
DMSO	VRSA	Biofilm/animal infection model	MIC MBC	156.25 μ g/mL	20 J/cm ²	[30]
N/R	<i>S. aureus</i>	Animal infection model	aPDT	78 μ g/mL	60 J/cm ²	[31]
DMSO	<i>S. aureus</i>	Infected fruit	Survival fraction	100 nM	1.5 and 9 J/cm ²	[32]
N/R	<i>S. aureus</i> <i>E. coli</i>	Planktonic	PDI	40 and 80 μ M	15 J/cm ²	[33]
Tween 80 (0.5%)	<i>S. aureus</i>	Planktonic	CFU/mL	300 and 500 μ M	0.03–0.05 W/cm ²	[34]
N/R	<i>S. aureus</i>	Biofilm	Confocal microscope	N/R	170 μ mol m ² s ⁻¹	[35]
DMSO (0.5%)	<i>S. aureus</i>	Biofilm	SDT aPDT SPDT	80 μ M	100 Hz 15 and 70 J/cm ² 100 Hz, 15 and 70 J/cm ²	[36]
DMSO	<i>E. coli</i>	Planktonic	MIC Inhibition zone	110, 220 and 330 μ g/mL	-	[37]

Solvent	Microorganism	Culture	Antimicrobial Method	CUR Concentration	Light/Ultrasonic Parameters	Reference
DMSO	<i>E. coli</i>	Planktonic	OD _{600nm}	8,16, 32, and 64 µg/mL	-	[38]
N/R	<i>S. dysenteriae</i> <i>C. jejuni</i>	Planktonic	MIC/MBC	256 and 512 µg/mL	-	[39]
Edible alcohol	<i>E. coli</i>	Planktonic	aPDT	5, 10, and 20 µM	3.6 J/cm ²	[40]
DMSO	<i>H. pylori</i>	Planktonic biofilm	MIC MBC aPDT	50 µg/mL	10 mW/cm ²	[41]
DMSO	<i>P. aeruginosa</i>	Biofilm	aPDT CFU/mL	N/R	5 and 10 J/cm ²	[42]
DMSO	Imipenem-resistant <i>A. baumannii</i>	Planktonic	aPDT	25, 50, 100, and 200 µM	5.4 J/cm ²	[43]
DMSO (2%)	<i>P. aeruginosa</i> , <i>A. baumannii</i> , <i>K. pneumoniae</i> , <i>E. coli</i> , <i>E. faecalis</i>	Planktonic	MIC/FICI	128-256 µg/mL	-	[44]
N/R	<i>C. difficile</i> , <i>C. sticklandii</i> , <i>B. fragilis</i> , <i>P. bryantii</i>	Planktonic	Viable cell number	10 µg/mL	-	[45]
N/R	<i>B. subtilis</i> , <i>E. coli</i> , <i>S. carnosus</i> , <i>M. smegmatis</i>	Planktonic	MIC/MBC	Up to 25 µM	-	[46]
N/R	MRSA MSSA <i>E. coli</i>	Planktonic/animal infection model	MIC	4–16 µg/mL 2–8 µg/mL 8–32 µg/mL	-	[47]
N/R	<i>E. faecalis</i> , <i>S. aureus</i> , <i>B. subtilis</i> , <i>P. aeruginosa</i> , <i>E. coli</i>	Planktonic	MIC	156 µg/mL	-	[48]
DMSO (0.5%)	<i>A. hydrophila</i> , <i>E. coli</i> , <i>E. faecalis</i> , <i>K. pneumoniae</i> , <i>P. aeruginosa</i> , <i>S. aureus</i> , <i>C. albicans</i>	Planktonic	MIC/MBC/ FICI/aPDT	37.5–150 µg/mL	N/C	[49]
N/R	<i>E. faecalis</i>	Infection model	CFU/mL	1 µg/mL	-	[50]

Solvent	Microorganism	Culture	Antimicrobial Method	CUR Concentration	Light/Ultrasonic Parameters	Reference
Commercial solution	<i>E. faecalis</i>	Biofilm	aPDT	1.5 g/mL	20.1 J/cm ²	[51]
Ethanol 99%	<i>A. hydrophila</i> , <i>V. parahaemolyticus</i>	Planktonic	aPDT/SDT	Up to 15 mg/L	N/C	[52]
DMSO (10%)	<i>E. faecalis</i>	Biofilm	MIC/MBC	120 mg/mL	-	[53]
N/R	<i>S. mutans</i>	Planktonic	aPDT	10 g/100cc	N/C	[54]
DMSO: ethyl alcohol	<i>S. mutans</i> , <i>S. pyogenes</i>	Planktonic	aPDT	3 mg/mL	28.8 J/cm ²	[55]
DMSO (0.8%)	Caries isolated	Biofilm	aPDT	600 µg/mL	75 J/cm ²	[56]
DMSO	<i>S. mutans</i> , <i>C. albicans</i>	Biofilm single/dual	MBEC	0.5 mM	-	[57]
DMSO (0.05 M)	<i>A. actinomycetemcomitans</i>	Planktonic	aPDT	40 µg/mL	300–420 J/cm ²	[58]
DMSO (<1%)	<i>P. gingivalis</i> , <i>A. actinomycetemcomitans</i>	Planktonic	aPDT	20 µg/mL	6, 12 or 18 J/cm ²	[59]
DMSO (0.5%)	<i>P. gingivalis</i> , <i>A. actinomycetemcomitans</i> , <i>C. rectus</i> , <i>E. corrodens</i> , <i>F. nucleatum</i> , <i>P. intermedia</i> , <i>P. micra</i> , <i>T. denticola</i> , <i>T. forsythia</i>	Biofilm	aPDT	100 mg/L	-	[60]
N/R	Subgingival plaque	Biofilm	aPDT	100 µg/mL	30 J/cm ²	[61]
DMSO	<i>P. gingivalis</i>	Planktonic	MIC	12.5 µg/mL	-	[62]
Ethanol: DMSO (99.9%: 0.1%)	Periodontal pocket	-	aPDT	100 mg/mL	7.69 J/cm ²	[63]
Tween 80	<i>Streptococcus</i> spp, <i>Staphylococcus</i> spp, <i>Enterobacteriaceae</i> , <i>C. albicans</i>	Clinical trail	aPDT	0.75 mg/mL	20.1 J/cm ²	[64]
Sodium hydroxide:	<i>C. albicans</i> , <i>C. parapsilosis</i> , <i>C.</i>	Planktonic/biofilm	MIC	0.1–0.5 mg/mL	-	[65]

surrogate of the human herpesvirus, [20]. CUR was able to inhibit the type replication of Kaposi's sarcoma-associated herpesvirus (KSHV) as well as reduce its pathogenesis (neoangiogenesis and cell invasion of KSHV-infected mesenchymal stem cell from the periodontal ligament) [21].

While the antiviral effect of CUR has been experimentally demonstrated, the effect of CUR against the new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the etiologic agent of COVID-19, has been predicted by in silico studies using computational techniques, such as molecular docking [75][76][77][78][79][80][81][82]. These in silico studies showed the binding affinity of CUR to the spike protein of SARS-CoV-2 and the human receptors of the host cell, which could inhibit the viral infection into the human cells. The targets to which CUR may bind are the viral non-structural protein 9 (Nsp9) [77] and 15 (Nsp15) [81], main proteases of SARS-CoV-2 (important for viral

Solvent	Microorganism	Culture	Antimicrobial Method	CUR Concentration	Light/Ultrasonic Parameters	Reference
PBS	<i>glabrata</i> , <i>C.dubliniensis</i>					
N/R	<i>C. albicans</i> , <i>S. aureus</i>	Planktonic Biofilm	MIC/Biofilm percentag	200 µg/mL	-	
N/R	<i>C. albicans</i>	Biofilm	aPDT	1.5 g/mL	20.1 J/cm ²	
DMSO (10%)	<i>C. albicans</i>	Biofilm	aPDT	20, 40, 60 and 80 µM	2.64, 5.28, 7.92, 10.56, and 13.2 J/cm ²	
DMSO (1%)	<i>C. albicans</i>	Biofilm	aPDT	40 and 80 mM	37.5 and 50 J/cm ²	
N/R	<i>C. albicans</i>	Biofilm	aPDT	100 µM	10 J/cm ²	
DMSO (2.5%)	Fluconazole-resistant <i>C. albicans</i>	Planktonic/biofilm/infection model	MIC/ aPDT	40 µM	5.28 J/cm ²	
	Fluconazole-susceptible <i>C. albicans</i>			80 µM	40.3 J/cm ²	
DMSO	<i>C. albicans</i> , <i>F. oxysporum</i> , <i>A. flavus</i> , <i>A. niger</i> , <i>C. neoformans</i>	Planktonic	MIC	137.5–200 µg/mL	-	

2.2. Antibacterial Activity

The antibacterial effect of CUR has been demonstrated against Gram-positive and Gram-negative species, including strains responsible for human infections and showing antibiotic resistance [11][16][85][86]. CUR also inhibits bacterial biofilms, which are communities of cells embedded in a self-produced polymeric matrix tolerant to antimicrobial treatments [11][16][85][86]. The antibacterial mechanism of action of CUR involves damage to the cell wall or cell membrane, interference on cellular processes by targeting DNA and proteins, and inhibition of bacterial quorum sensing (communication process mediated by biochemical signals that regulate cell density and microbial behavior) [85]. Moreover, CUR affected the L-tryptophan metabolism in *Staphylococcus aureus* (Gram-positive) but not in *Escherichia coli* (Gram-negative), produced lipid peroxidation, and increased DNA fragmentation in both bacteria [26]. These results, along with the increased levels of total thiol and antioxidant capacity observed after bacterial cells were treated with CUR, suggested that oxidative stress may be the mechanism of antibacterial action of CUR [26]. Therefore, these multiple targets make CUR an interesting option for antibiotic-resistant strains. CUR is effective in killing methicillin-resistant *S. aureus* (MRSA), which is a concerning pathogen responsible for nosocomial and community-associated infections [86]. CUR and another polyphenol, quercetin, inhibited the growth of MRSA and their combination was synergistic [27]. Moreover, CUR absorbs blue light (400–500 nm) and is used as a natural photosensitizer (PS) in antimicrobial Photodynamic Therapy (aPDT) [87]. CUR-mediated aPDT reduced the viability of reference strain of *S. aureus* and clinical isolates of methicillin-sensitive *S. aureus* (MSSA) and MRSA by 4 log₁₀, while CUR alone reduced their survival by 2 log₁₀ [28]. The aPDT mediated by CUR in 10% DMSO reduced the biofilm viability of *S. aureus* and MRSA by 3 and 2 log₁₀, respectively, and their metabolic activity by 94% and 89%, respectively [29]. The antibiofilm activity of CUR-mediated aPDT was also observed against clinical isolates of vancomycin-resistant *S. aureus* (VRSA), with reductions of 3.05 log₁₀ in biofilm viability, 67.73% in biofilm biomass, and 47.94% in biofilm matrix [30]. Additionally, aPDT resulted in the eradication

of VRSA in a rat model of skin infection [30]. The association of CUR-mediated aPDT with artificial skin resulted in a 4.14 log₁₀ reduction in *S. aureus* from infected wounds in rats [31].

The combination of CUR and another natural PS, hypocrellin B, increased the photoinactivation of *S. aureus* compared with the photodynamic effect of each PS alone [32]. Bacterial cells showed alteration in their membrane integrity and the dual-PS-mediated aPDT also decontaminated apples with *S. aureus* [32]. The CUR-mediated aPDT was also effective in decontaminating food, reducing the number of *S. aureus* recovered from meat and fruit [33]. Compared to another natural PS, aloe-emodin, CUR was less effective in photokilling *S. aureus* and *E. coli* [34]. Three-dimensional cages fabricated with CUR and resin monomer (pentaerythritol triacrylate) polymerized by infrared light were used to entrap and kill *S. aureus*. Irradiation of cages for 10 min with visible light resulted in a bacteria mortality rate of 95% [35]. Following the principles of aPDT, Sonodynamic Therapy (SDT) associates a PS (also called sonosensitizer) with ultrasound (US) instead of light for the treatment of deeper lesions and infections, where light cannot reach [88]. Both aPDT and SDT mediated by CUR, as well as the combination of both (SPDT, when the PS is activated by light and US simultaneously), reduced the viability of *S. aureus* biofilms. SPDT promoted the highest reduction (3.48 log₁₀), which was potentiated when CUR was combined with sodium dodecyl sulfate (7.43 log₁₀) [36]. Regarding Gram-negative species, CUR alone was not able to inhibit the growth of an Enterotoxigenic *E. coli*, which is a strain that causes severe diarrhea and is resistant to antibiotics [37]. However, synergism was observed between CUR at 330 µg/mL and antibiotics (Ceftazidime, Amoxicillin/Clavulanic acid, Cefotaxime, and Ampicillin) [37]. CUR did not affect the growth of enteroaggregative (EAEC) and enteropathogenic (EPEC) diarrheagenic *E. coli* but inhibited the secretion and release of their virulence factors, Pet and EspC, which are toxins produced by these strains [38]. Conversely, CUR alone and with ampicillin inhibited the growth of other species that caused diarrhea—*Shigella dysenteriae* and *Campylobacter jejuni*, including multidrug-resistant strains [39]. The aPDT mediated by CUR and light reduced the viability of *E. coli* by 3.5 log, increased membrane permeability of bacteria, and decontaminated oysters [40]. CUR-mediated aPDT reduced the viability of *Helicobacter pylori* and its virulence factors (motility, urease production, adhesion to erythrocytes, and biofilm formation) [41]. On *Pseudomonas aeruginosa*, aPDT potentiated the inhibitory effect of CUR, inhibited biofilm formation and matrix production, reduced biofilm thickness, and downregulated quorum sensing genes [42]. The photoinactivation of imipenem-resistant *Acinetobacter baumannii* reduced bacterial viability by 97.5% and shotgun proteomics analysis identified 70 carbonylated proteins modified after CUR mediated aPDT related to the membrane, translation, and response to oxidative stress [43]. CUR inhibited the growth of antibiotic-resistant *P. aeruginosa*, *A. baumannii*, and *Klebsiella pneumoniae* isolated from burn wound infections and showed synergism with meropenem [44]. On gastrointestinal bacteria of human and bovine origin, CUR inhibited Firmicutes (*Clostridioides difficile* and *Acetanaerobium (Clostridium) sticklandii*) but did not affect Bacteroidetes (*Bacteroides fragilis* and *Prevotella bryantii*) [45]. CUR was conjugated to triphenyl phosphonium resulting in a compound named Mitocurcumin, which inhibited the growth of *Bacillus subtilis*, *E. coli*, *Staphylococcus carnosus*, and *Mycobacterium smegmatis*, and induced morphological changes in *B. subtilis* [46]. Seventeen synthesized monocarbonyl curcuminoids showed high antibacterial activity against MSSA and MRSA and moderate activity against *E. coli* [47]. The four most effective curcuminoids were bacteriostatic at low concentrations and bactericidal at high concentrations against MRSA, which showed membrane damage. In an ex vivo mammalian co-culture infection model, two curcuminoids

decreased the viability of MSSA internalized in the fibroblasts [47]. One of thirteen synthesized curcuminoids, 3,30-dihydroxycurcumin, showed antibacterial activity against *S. aureus*, *B. subtilis*, *Enterococcus faecalis*, and *Mycobacterium tuberculosis*, and produced membrane damage on *B. subtilis* [48]. Nonetheless, all the synthesized curcuminoids were not effective against Gram-negative species (*P. aeruginosa* and *E. coli*) [48]. CUR analogs (monocurcuminoids, MC) were synthesized and showed higher, lower, or similar antimicrobial activity than CUR against *Aeromonas hydrophila*, *E. coli*, *E. faecalis*, *K. pneumoniae*, *P. aeruginosa*, *S. aureus*, and the yeast *Candida albicans* [49]. Two MC and turmeric powder presented synergism against *A. hydrophila*, *P. aeruginosa*, and *C. albicans*. When aPDT was performed with UV light, two MC-mediated aPDT decreased the growth of *E. faecalis*, *E. coli*, and *S. aureus*, while aPDT with another MC and CUR increased the growth of *A. hydrophila*, *E. faecalis*, *S. aureus*, *C. albicans*, and *P. aeruginosa* [49]. CUR was more effective than other natural biomolecules (quercetin and resveratrol) in inhibiting the growth of *E. faecalis* in spermatozoa from rabbits, but less effective than antibiotics [50]. CUR-mediated aPDT also reduced the viability of *E. faecalis* biofilms grown in bovine bone cavities for 14 days by 1.92 log₁₀ [51]. The aPDT and the combination of a nanobubble solution and the US reduced the viability of the aquatic pathogens *Aeromonas hydrophila* and *Vibrio parahaemolyticus* [52].

CUR and aPDT have been used for dental infections and oral diseases. The *Curcuma longa* extract decreased the viability of 3-week-old *E. faecalis* biofilms formed on the root canal surface of human teeth [53]. The aPDT mediated by CUR and continuous laser irradiation eradicated planktonic cultures of *Streptococcus mutans*, which is the main etiologic factor of dental caries [54]. A formulation of syrup with curcuminoids and 30% sucrose was used as a PS in aPDT, which reduced the viability of *S. mutans*, *Streptococcus pyogenes*, and a clinical isolate from a patient with pharyngotonsillitis [55]. Microbial samples from carious dentin were grown as microcosm biofilm and submitted to CUR-mediated aPDT, which reduced the vitality of 3- and 5-day-old biofilms [56]. CUR alone decreased the biomass and the viability of mono- and dual-species biofilms of *S. mutans* and *C. albicans*, as well as the production of biofilm matrix and the expression of genes related to glucosyltransferase and quorum sensing of *S. mutans*, and the adherence of *C. albicans* [57]. The therapeutic effect of CUR on periodontal diseases was extensively investigated in animal models and clinical trials, which were reviewed [89]. Beyond its antibacterial activity, CUR-mediated aPDT also produced a bystander effect (behavior change of cells exposed to treated target cells) on the periodontal pathogen *Aggregatibacter actinomycetemcomitans*, reducing its survival, metabolic activity, and the production of quorum sensing molecule [58]. The aPDT with CUR decreased the growth of both *A. actinomycetemcomitans* and *Porphyromonas gingivalis*, which is another pathogenic periodontal bacterium [59]. Antimicrobial photothermal treatment promoted higher reduction than CUR-mediated aPDT in the viability of mixed biofilms of periodontal pathogens (*P. gingivalis*, *A. actinomycetemcomitans*, *Campylobacter rectus*, *Eikenella corrodens*, *Fusobacterium nucleatum*, *Prevotella intermedia*, *Parvimonas micra*, *Treponema denticola*, and *Tannerella forsythia*) grown on a titanium surface inside artificial periodontal pockets [60]. The aPDT mediated by different PS (methylene blue, CUR, and chlorin e6) eradicated the planktonic growth and reduced the biofilm viability of metronidazole-resistant bacteria from the subgingival plaque [61]. CUR alone inhibited the growth of *P. gingivalis* and CUR in gel was biocompatible when evaluated subcutaneously in rats [62].

A randomized clinical trial showed that CUR-mediated aPDT associated with scaling and root planing improved the clinical attachment level gain of periodontal pockets in type-2 diabetic patients after three and six months [63]. The

aPDT with CUR and LED applied in the mouth of 30 patients with acquired immune deficiency syndrome (AIDS) reduced the counts of *Streptococcus* spp., *Staphylococcus* spp., and total microorganisms from saliva, but not the number of Enterobacteriaceae and *Candida* spp. [64]. Additionally, there was no reduction in patients with CD8 lymphocytes lower than 25% [64].

2.3. Antifungal Activity

The antifungal activity of CUR has been demonstrated mostly against *Candida* spp. by many in vitro and few in vivo studies [90]. CUR inhibited the growth of a reference strain and a clinical isolate of *C. albicans*, as well as reference strains of *Candida parapsilosis*, *Candida glabrata*, and *Candida dubliniensis* [65]. When biofilms of both *C. albicans* strains were evaluated, CUR reduced only the viability of the standard strain in a concentration-dependent effect, while the antifungal fluconazole did not inhibit the viability of either strain [65]. CUR and 2-aminobenzimidazole (2-ABI) inhibited the growth and adhesion of *C. albicans* and *S. aureus* to medical-grade silicone [66]. The combination of CUR and 2-ABI enhanced the inhibition of biofilm formation and reduced the viability of 48 h-old single and dual-species biofilms [66]. The aPDT mediated by CUR reduced the survival of 14-day-old biofilm of *C. albicans* in bone cavities, confirmed by fluorescence spectroscopy [67]. CUR-mediated aPDT reduced the metabolic activity of biofilms of *C. albicans* reference strain and clinical isolates from the oral cavity of patients with HIV and lichen planus [68]. Moreover, genes related to hyphae and biofilm formation were downregulated [68]. The aPDT mediated by CUR and another PS, Photodithazine®, also resulted in the downregulation of genes involved in adhesion and oxidative stress response in *C. albicans* biofilms [69]. CUR alone and CUR-mediated aPDT, combined or not with an antibody-derived killer decapeptide, reduced the metabolic activity of an 18 h biofilm of *C. albicans* [70]. CUR showed synergism with fluconazole and CUR-mediated aPDT inhibited the planktonic growth and reduced the biofilm viability of fluconazole-resistant *C. albicans* [71]. CUR-mediated aPDT also increased the survival of *Galleria mellonella* infected with fluconazole-susceptible *C. albicans*, but did not affect the survival of larvae infected with fluconazole-resistant strain [71]. A library of 2-chloroquinoline incorporated monocarbonyl curcuminoids (MACs) was synthesized and most of the MACs exhibited strong or moderate antifungal activity compared with miconazole against *C. albicans*, *Fusarium oxysporum*, *Aspergillus flavus*, *Aspergillus niger*, and *Cryptococcus neoformans* [72]. To suggest a possible antifungal mechanism, a molecular docking analysis showed that MACs had binding affinity to sterol 14 α -demethylase (CYP51), leading to impaired fungal growth [72].

3. Curcumin in DDSs (Colloidal, Metal, and Hybrid Nanosystems)

3.1. CUR in Micelles

Micelles are aggregates of surfactants or block polymers self-assembled in water solution. They are used as DDSs and formed by a hydrophilic domain named corona and a hydrophobic domain called core (Figure 1) [91], which stays in contact with hydrophobic drugs such as CUR [91]. Micelles have low toxicity, biocompatibility, and

sustained release, which makes them an attractive DDS to carry CUR and to be used in medical applications [91]. Antimicrobial studies with CUR-loaded micelles are summarized in **Table 2**.

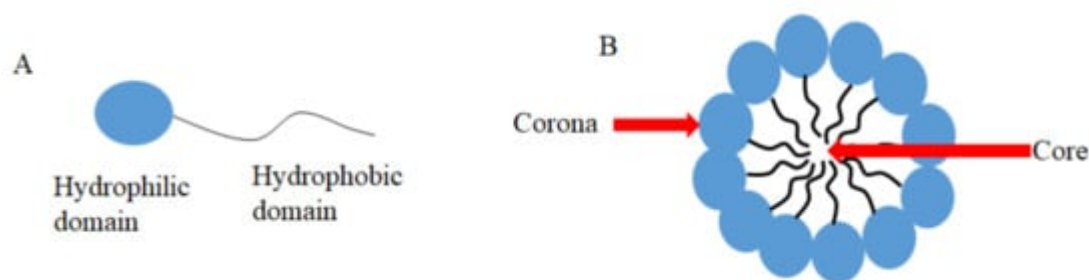


Figure 1. Schematic representation of: (A) an amphiphilic molecule and (B) an assembled micelle.

Table 2. Antimicrobial studies performed with CUR in micelles.

Type of Micelles	[CUR] Formulation	Microorganism	Type of Culture	Antimicrobial Method	Antimicrobial [CUR]	Light/Ultrasonic Parameters	Reference
Mixed polymer micelles	1000 ppm	<i>E. coli</i> , <i>S. aureus</i> , <i>A. niger</i>	Planktonic	MIC	350 and 275 µg/mL	-	[92]
PCL- <i>b</i> -PASP and Ag	2 mg/mL	<i>P. aeruginosa</i> , <i>S. aureus</i>	Planktonic	OD _{600nm}	8–500 µg/mL	-	[93]
mPEG-OA	1:10	<i>P. aeruginosa</i>	Planktonic	MIC	400 µg/mL	-	[94]
PEG-PCL	10 mg	<i>C. albicans</i>	Planktonic	MIC	256 µg/mL	-	[95]
PEG-PE	50 mM	<i>S. mutans</i>	Planktonic	SACT	50 mM	1.56 W/cm ²	[96]
DAPMA, SPD, SPM	0.32 mg/mL	<i>P. aeruginosa</i>	Planktonic	OD _{600nm} and aPDT	250, 500 nM, 1 µM and 50, 100 nM	18 and 30 J/cm ²	[97]
P123	0.5% w/V	<i>S. aureus</i>	Planktonic	aPDT	7.80 µmol/L	6.5 J/cm ²	[98]
PCL- <i>b</i> -PHMG- <i>b</i> -PCL, STES	10 mg	<i>S. aureus</i> , <i>E. coli</i>	Planktonic	MIC	16 and 32 µg/mL *	-	[99]
CUR-PLGA-DEX	1 mg/mL	<i>P. fluorescens</i> , <i>P. putida</i>	Planktonic biofilm	OD _{600nm} antibiofilm	0.625–5 mg/mL	-	[100]

3.2. CUR in Liposomes

Liposomes are biodegradable and biocompatible systems, which consist of hydrophobic and hydrophilic groups (Figure 2) [101]. The hydrophobic layer is mainly composed of phospholipids and cholesterol molecules. This lipid-based carrier is suitable for administering water-insoluble drugs, such as CUR [102]. Liposomes are classified into three groups: single unilamellar vesicles, large unilamellar vesicles, and multilamellar vesicles [103]. Drugs encapsulated in liposomes are protected from chemical degradation and show increased drug solubility [101]. Additionally, liposomes have advantageous properties such as better penetration into the skin, deposition, anti-melanoma, and antimicrobial activity [102]. Antimicrobial studies with CUR-loaded liposomes are summarized in Table 3.



3.11. CUR in Films, Hydrogels, and Other Nanomaterials

2. Schematic representation of the liposome structure.

Antimicrobial studies with CUR in films, hydrogels, and other nanomaterials are summarized in Table 11.

Table 3. Antimicrobial studies performed with CUR in liposomes and solid lipid nanoparticles (SLN).

Table 11. Antimicrobial studies performed with CUR in films, hydrogels, and other nanomaterials.

Type of Liposomes or	[CUR]	Microorganism	Type of Culture	Antimicrobial Method	Antimicrobial [CUR]	Light/Ultrasonic Parameters	Antimicrobial Reference
Type of Material	[CUR] Formulation	Microorganism	Type of Culture	Antimicrobial Method	Antimicrobial [CUR]	Light/Ultrasonic Parameters	Reference
CuR-SiNPs	20 mg	<i>S. aureus</i> , <i>P. aeruginosa</i>	Planktonic, Biofilm	aPDT	50 µg/mL, 1 mg/mL	20 J/cm ²	[210] [104]
CUR-HNT-DX	10 mg	<i>S. marcescens</i> , <i>E. coli</i>	Planktonic, Infection model	Grown inhibition, Confocal microscopy	Up to 0.5 mg/mL	-	[211] [105]
Exosomes	N/R	HIV-1 infection	-	Flow cytometry	N/R	-	[212]
Electrospun nanofibers	100 mg/mL	<i>Actinomyces naeslundii</i>	Biofilm	aPDT	2.5 and 5 mg/mL	1200 mW/cm ²	[213]
Ga NFCD-GO NF	0.1 mol	<i>B. cereus</i> , <i>E. coli</i>	Planktonic	Zone of inhibition, MIC	Up to 63.25 µg/mL	-	[214] [106]
PLGA: triglycerides: F68	0.8 mg/mL	<i>E. coli</i> , <i>S. typhimurium</i> , <i>P. aeruginosa</i> , <i>S. aureus</i> , <i>B. sonorensis</i> ,	Planktonic	MIC	75 and 100 µg/mL		[107]

Multinano-fibers-film	1, 2.5, and 5 mg/mL	<i>S. aureus</i> <i>E. coli</i>	Planktonic	UFC/mL, Confocal microscopy	1 mg/mL	-	[215]	ference
Nanofibers scaffolds	4.0 wt%	<i>S. aureus</i> <i>Pseudomonas</i> ssp.	Planktonic	Colony count	N/R	,-	[216]	[104]
Nanofibrous scaffold	5%	<i>S. aureus</i> , <i>E. coli</i>	Planktonic	Colony count	20 mg	-	[217]	
Nanofibers	5 and 10%wt	<i>S. aureus</i> <i>E. coli</i>	Planktonic	OD _{600nm}	Up to 212.5 µg/mL	-	[218]	
CSDG	1 w/w	<i>S. aureus</i> , <i>E. coli</i>	Planktonic, Infection model	Colony count, Microscopy	N/R	-	[219]	[108]
Gelatin film	0, 0.25, 0.5, 1.0, and 1.5 wt%	<i>E. coli</i> , <i>L. monocytogenes</i>	Planktonic	UFC/mL	0.25 and 1.5 wt%	-	[220]	tant and
ZnO-CMC film	0.5 and 1.0 wt%	<i>E. coli</i> , <i>L. monocytogenes</i>	Planktonic	UFC/mL	1 wt%	-	[221]	CUR and
Pectin [220]	40 mg	<i>E. coli</i> , <i>L. monocytogenes</i>	Planktonic	UFC/mL	N/R	-	[222]	resistant
Edible film	0.4% (w/v)	<i>E. coli</i> , <i>B. subtilis</i>	Planktonic	Zone of inhibition	1% wt.	-	[223]	eatment, to study

avoiding over- or under-estimation of interactions. For example, while the time–kill curve of *C. jejuni* treated with

3.3. CUR in Solid Lipid Nanoparticles

Both cinnamon oil and ZnO NPs resulted in the over-estimation of synergism between the antimicrobials, the fractional inhibitory concentration index (FICI) method showed no synergism but only an additive effect [225]. The Solid lipid nanoparticles (SLN, Figure 3, Table 3) are a modern type of lipid-based carrier composed by solid FICI method was not able to detect the synergism between binary combinations of antimicrobials (cinnamon oil, biodegradable lipids and spherical solid lipid particles. SLNs are water colloidal or aqueous surfactant solution ZnO NPs, and CUR encapsulated in starch) at sub-MIC, which resulted in the non-turbidity of *C. jejuni*. In turn, systems [102]. SLNs have advantages such as biocompatibility, biodegradability, greater drug absorption, and drug mathematical modeling using isobolograms and median-effect curves showed synergism when CUR in starch was retention [18][102], thus they are an interesting system to carry CUR [14]. Currently, SLNs have become popular combined with other antimicrobials against *C. jejuni*, with bacterial reductions of 3 log for the binary combination because they are used as carriers for COVID-19 vaccines based on RNA vaccine technology (Moderna and Pfizer–BioNTech). antimicrobial responsible for the synergistic interaction [225].

In addition to the antimicrobial evaluation, in vitro and in vivo studies have demonstrated the cytocompatibility and biocompatibility of CUR in DDSs [108][113][114][115][118][121][144][145][152][156][168][185][192][202][209], suggesting that CUR-loaded DDSs might be safe. Although a plethora of DDSs has been developed to circumvent the hydrophobicity, instability in solution, and low bioavailability of CUR, several studies are still performed with free CUR dissolved in organic solvents [19][20][21][22][23][24][25][26][27][28][29][30][31][32][33][34][35][36][37][38][39][40][41][42][43][44][45][46][47][48][49][50][51][52][53][54][55][56][57][58][59][60][61][62][63][64][65][66][67][68][69][70][71][72][85][86][87][88][89][90]. Furthermore, compared to several in vitro investigations, few in vivo studies using animal infection models and scarce clinical trials have been reported. A randomized clinical trial showed that aPDT mediated by free CUR improved gingivitis in adolescents under fixed orthodontic treatment but did not reduce dental plaque accumulation after 1 month [226]. Clinical improvements after CUR-mediated aPDT were also observed for periodontal diseases, although few studies have evaluated the microbiological parameters [63][89]. Therefore, the improvement of clinical parameters might be due to the anti-

inflammatory effect of CUR/aPDT instead of their in vivo antimicrobial activity. Nonetheless, randomized clinical trials evaluating CUR in DDSs against infections are required.

As a note on the future use of CUR, the incorporation of CUR in DDS and other pharmaceutical formulations allows its clinical use especially as an adjuvant agent to conventional antimicrobial agents. Such a combination can be an important weapon in the battle against resistant strains and emergent pathogens. The use of stimuli-responsive (or smart) DDS can also improve CUR delivery and its therapeutic effect on the target tissue. The combination of polymeric and metallic carriers may also enhance the therapeutic activity of CUR. Nonetheless, the degradation of DDS and its clearance from the body are other issues that require further investigation [18]. The evidence produced so far about the antimicrobial activity of CUR in DDSs supports future in vivo and clinical studies, which may pave the way for industrial production.

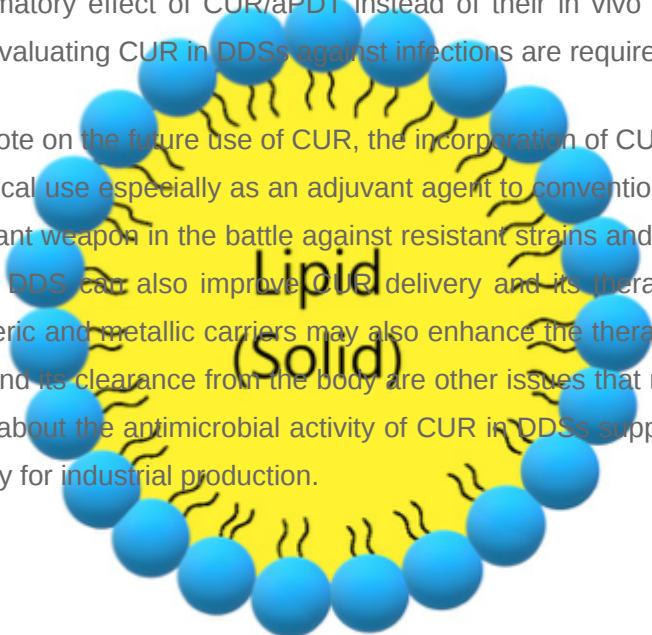


Figure 3. Schematic representation of solid lipid

References

nanoparticle.

- Charles E Davis; Antonella Rossati; Olivia Bargiacchi; Pietro Luigi Garavelli; Anthony J McMichael; Gunnar Juliusson; Globalization, Climate Change, and Human Health. *New England Journal of Medicine* **2013**, 369, 94-96, 10.1056/nejmc1305749.
- Lance Saker; Kelley Lee; Barbara Cannito; Anna Gilmore; Diarmid Campbell-Lendrum; Globalization and infectious diseases: a review of the linkages. *WHO Special Programme on Tropical Diseases Research* **2004**, 3, 3-12.
- Shaghayegh Gorji; Ali Gorji; COVID-19 pandemic: the possible influence of the long-term ignorance about climate change. *Environmental Science and Pollution Research* **2021**, 28, 15575-15579, 10.1007/s11356-020-12167-z.
- Jyoti Tanwar; Shrayanee Das; Zeeshan Fatima; Saif Hameed; Multidrug Resistance: An Emerging Crisis. *Interdisciplinary Perspectives on Infectious Diseases* **2014**, 2014, 1-7, 10.1155/2014/541340.
- Maya A. Farha; Eric D. Brown; Drug repurposing for antimicrobial discovery. *Nature Microbiology* **2019**, 4, 565-577, 10.1038/s41564-019-0357-1.
- Bradley S. Moore; Guy T. Carter; Mark Brönstrup; Editorial: Are natural products the solution to antimicrobial resistance? *Natural Product Reports* **2017**, 34, 685-686, 10.1039/c7np90026k.
- Thaís Soares Bezerra Santos Nunes; Leticia Matheus Rosa; Yuliana Vega-Chacón; Ewerton Garcia De Oliveira Mima; Fungistatic Action of N-Acetylcysteine on *Candida albicans* Biofilms and Its Interaction with Antifungal Agents. *Microorganisms* **2020**, 8, 980, 10.3390/microorganisms8070980.

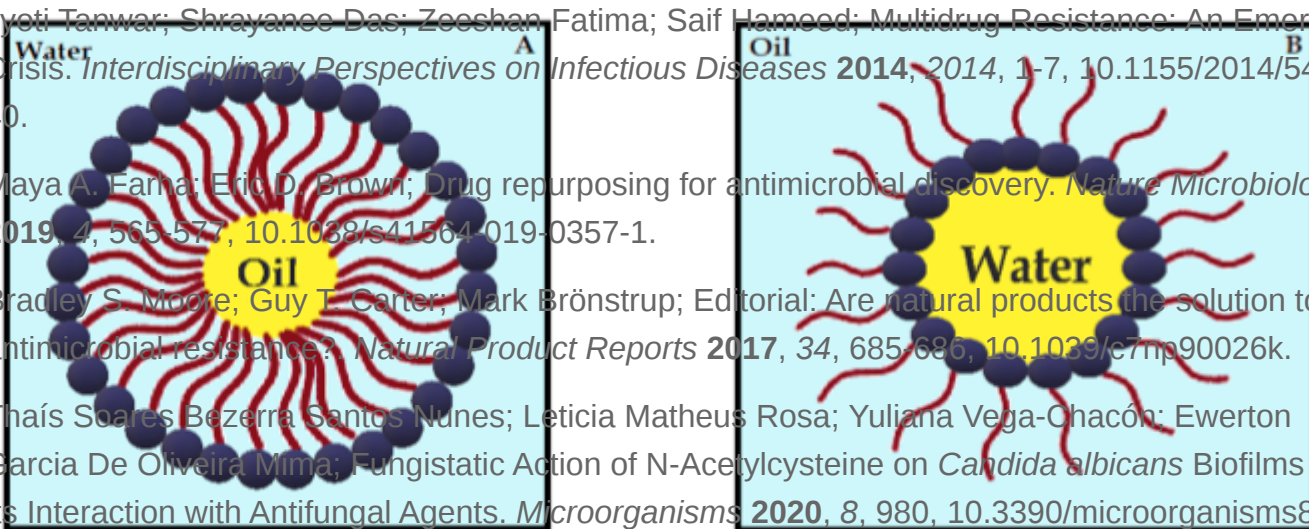


Figure 4. Schematic diagram of oil-in-water nanoemulsion (A) and water-in-oil nanoemulsion (B), stabilized by surfactants.

8. Susan J. Helwig; Douglas S. Kadam; Curcumin: A Review of its Effects on Human Health. *Foods* **2017**, 6, 92, 10.3390/foods6100092.

Type of Emulsion	[CUR] Formulation	Microorganisms	Type of culture	Antimicrobial method	Antimicrobial Concentration	Light/Ultrasonic Paramet	Reference	Lessons
THC ME	5%	HIV-1	Cell infection	IC ₅₀	0.9357 µM	-	[113]	as
CUR-NE	N/R	HPV	-	aPDT	80 µM	50 J/cm ²	[114]	ns2005
CUR-NE	N/R	DENV-1 to 4	Cell infection	Cell viability	1, 5, 10 µg/mL	-	[115]	and
P60-CUR	4 mg/L	<i>E. coli</i>	Planktonic	OD595 nm	N/R	-	[116]	
PE:CUR	0.566 mg/mL	<i>S. aureus</i> , <i>S. epidermidis</i> , <i>S. faecalis</i> , <i>C. albicans</i> , <i>E. coli</i>	Planktonic	Inhibition zone	1 mg/mL*	-	[117]	Agent.
cu-SEDDS	1%	<i>E. aureus</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>K. pneumonia</i>	Planktonic	MIC	45–62 µg/mL	-	[118]	ug T.2019.
CUR:NE in microbeads	0.5 mg/mL	<i>E. coli</i> , <i>S. typhmerium</i> , <i>Y. enterocolitica</i> , <i>P. aeruginosa</i> , <i>S. aureus</i> , <i>B. cereus</i> , <i>L. monocytogenes</i>	Planktonic	Inhibition zone	90 and 180 mg/mL*	-	[119]	design
Lignin sulfomethylated	0.3 mg/mL	<i>S. aureus</i>	Planktonic	OD600 nm	2.4 mg/mL*	-	[120]	ry
C14-EDA/GM/WC14-MEDA/GM/W	N/R	<i>C. albicans</i>	Planktonic, biofilm	Microdilution assay, antibiofilm	100 µg/mL, 20 µg	-	[121]	jik; of

17. Anderson Clayton da Silva; Priscila Dayane De Freitas Santos; Jéssica Thais Do Prado Silva; Fernanda Vitória Leimann; Lívia Bracht; Odinei Hess Gonçalves; Impact of curcumin nanoformulation on its antimicrobial activity. *Trends in Food Science & Technology* **2018**, 72, 74–82, 10.1016/j.tifs.2017.12.004.
18. Simin Sharifi; Nazanin Fathi; Mohammad Yousef Memar; Seyed Mahdi Hosseiniyan Khatibi; Rovshan Khalilov; Ramin Negahdari; Sepideh Zununi Vahed; Solmaz Maleki Dizaj; Anti-microbial activity of curcumin nanoformulations: New trends and future perspectives. *Phytotherapy Research* **2020**, 34, 1926–1946, 10.1002/ptr.6658.

[CUR] = curcumin; [NE] = nanoemulsion; [aPDT] = active photodynamic therapy; [OD] = optical density; [MIC] = minimum inhibitory concentration. *: formulation concentration.

19. Yaning Gao; WanBo Tai; Ning Wang; Xiang Li; Shibo Jiang; Asim K. Debnath; Lanying Du; Shizhong Chen; Gao; Tai; et al. WangLiDuChen Identification of Novel Natural Products as Effective and Broad Spectrum Anti-Zika Virus Inhibitors. *Viruses* **2019**, 11, 1019, 10.3390/v11111019.
- 3.5. CUR in Cyclodextrin
- Cyclodextrins (CDs) have revolutionized the pharmaceutical industry in recent years. [121] CDs consist of three naturally occurring oligosaccharides in a cyclic structure produced from starch [123][124][125]. The natural CDs have their nomenclature system and their chemical structure based on the number of glucose residues in their structure:

20. Mayorga-Pedraza, M. A.; Morgan, V. M.; Doris, H. C.; Sepúlveda, A. Sensitization of the entire CD-hepatitis A virus and Talaromyces using grape seed extract, ginger and curcumin. *Food Microbiology* **2020**, 90, 103461, 10.1016/j.fm.2020.103461. hydrophilic layer and an internal hydrophobic cavity (Figure 5) [126]. They can sequester insoluble compounds within their hydrophobic cavity, resulting in better solubility and consequently better chemical and enzymatic stability. [124]. Due to the cavity size, β -CD forms inhibitor and exhibits an antiviral activity against KSHV replication and pathogenesis. *Antiviral Research* **2019**, 167, 98-103, 10.1016/j.antiviral.2019.04.011. appropriate inclusion complexes with molecules with aromatic rings [128], such as CUR [129]. Antimicrobial studies with CUR in CDs are summarized in Table 5.

22. Wael H. Roshdy; Helmy A. Rashed; Ahmed Kandeil; Ahmed Mostafa; Yassmin Moatasim; Omnia Kutkat; Noura M. Abo Shama; Mokhtar R. Gomaa; Ibrahim H. El-Sayed; Nancy M. El Guindy; et al. Amal Naguib Ghazi Kamil Mohamed A. Ali EGYVIR: An immunomodulatory herbal extract with potent antiviral activity against SARS-CoV-2. *PLOS ONE* **2020**, 15, e0241739, 10.1371/journal.pone.0241739.

Figure 5. Schematic representation of CUR in CD.

23. Chih-Chun Wen; Yuen-Hsiung Kuo; Jia-Tsong Jan; Po-Huang Liang; Sheng-Yang Wang; Hong-Gi Liu; Ching-Kuo Lee; Shang-Tzen Chang; Chih-Jung Kuo; Shoei-Sheng Lee; et al. Chia-Chung Hou-Pei-Wen Hsiao-Shih-Chang Chien-Lie-Fen Shyr-Ning-Sun Yang Specific Plant Terpenoids and Lignoids Possess Potent Antiviral Activities against Severe Acute Respiratory Syndrome Coronavirus. *Journal of Medicinal Chemistry* **2007**, 50, 4087-4095, 10.1021/jm070295s.

Type of CD	[CUR] Formulation	Microorganism	Type of Culture	Antimicrobial Method	Antimicrobial [CUR]	Light/Ultrasonic Parameters	Reference
PEG-based β -CD or γ -CD	10 μ M	<i>E. coli</i> , <i>E. faecalis</i>	Planktonic	aPDT	10 μ M	4.8, 29 J/cm ²	[130]
HPMC-stabilized hydroxypropyl- β -CD	7.64×10^{-3} M	<i>E. coli</i>	Planktonic	aPDT	10, 25 μ M	5, 14, 28 J/cm ²	[131]
methyl- β -CD hyaluronic acid HPMC	7.64×10^{-3} M	<i>E. faecalis</i> , <i>E. coli</i>	Planktonic	aPDT	0.5–25 μ M	11, 16, 32 J/cm ²	[132]
carboxymethyl- β -CD	20 μ M	<i>E. coli</i>	Planktonic	aPDT	0.7 ± 0.1 to 4.1 ± 1.6 nmole cm ⁻²	1050 ± 250 lx	[133]
hydrogel with CUR in hydroxypropyl- β -CD	15.8 mg/mL	<i>S. aureus</i>	Planktonic	Inhibition zone	2% (w/v)	-	[134]
α - and β -CD	1 mol/L	<i>E. coli</i> , <i>S. aureus</i>	Planktonic	MIC, OD600 nm	0.25 and 0.31 mg/mL	-	[135]

28. Mirian Aa Freitas; André Hc Pereira; Juliana G Pinto; Adriana Casas; Juliana Ferreira-Strixino; Bacterial viability after antimicrobial photodynamic therapy with curcumin on multiresistant *Staphylococcus aureus*. *Future Microbiology* **2019**, 14, 739-748, 10.2217/fmb-2019-0042.

29. Camilo Geraldo De Souza Teixeira; Paula Volpato Sanitá; Ana Paula Dias Ribeiro; Luana Mendonça Dias; Janaina Habib Jorge; Ana Cláudia Pavarina; Antimicrobial photodynamic therapy

β-CD or γ-CD in CS	0.06 mM	<i>E. coli</i> , <i>S. aureus</i>	Planktonic	MIC, Zone of inhibition	64 and 32 µg/mL	-	[136]
γ-CD	25 mg/L	<i>T. rubrum</i>	Planktonic	MIC, aPDT	N/R	45 J/cm ²	[137]
hydroxypropyl-β-CD	1:1	<i>B. subtilis</i> , <i>S. aureus</i> , <i>S. pyrogenes</i> , <i>P. aeruginosa</i> , <i>C. difficile</i> , <i>C. butyricum</i> , <i>L. monocytogenes</i> , <i>E. faecalis</i> , <i>E. coli</i> , <i>K. pneumoniae</i> , <i>P. mirabilis</i> , <i>S. typhimurium</i> , <i>E. aerogens</i> , <i>C. kusei</i> , <i>C. albicans</i>	Planktonic	Inhibition zone	25 mg/mL	-	[138]
methyl-β-CD	20 mM	<i>E. coli</i>	Planktonic	MIC, MBC, aPDT	500, 90 µM	9 J/cm ²	[139]

Biotechnology 2021, 14, 692–707, 10.1111/1751-7913.13734.

33. Thaila Quatrini Corrêa; Kate Cristina Blanco; Érica Boer Garcia; Shirly Marleny Lara Perez; Daniel José Chianfrone; Vinicius Sigari Moraes; Vanderlei Salvador Bagnato; Effects of ultraviolet light and curcumin-mediated photodynamic inactivation on microbiological food safety: A study in meat and fruit. *Photodiagnosis and Photodynamic Therapy* 2020, 30, 101678, 10.1016/j.pdpdt.2020.101678 [CUR] concentration. -: not performed. N/R: not reported.

34. Truong Dang Le; Pimonpan Phasupan; Loc Thai Nguyen; Antimicrobial photodynamic efficacy of selected natural photosensitizers against food pathogens: Impacts and interrelationship of process parameters. *Photodiagnosis and Photodynamic Therapy* 2020, 32, 102024, 10.1016/j.pdpdt.2020.102024

35. Davy-Louis Versace; Gabriela Moran; Mehdi Belqat; Arnaud Spangenberg; Rachel Meallet-Renault; Samir Abbad Andaloussi; Vlasta Brezova; Jean-Pierre Malval; Highly Virulent Bactericidal Effects of Curcumin-Based p-Cages Fabricated by Two-Photon Polymerization. *ACS Applied Materials & Interfaces* 2020, 12, 5050–5057, 10.1021/acsami.9b18693. [140][141] Moreover, CS is soluble in aqueous solutions and is the only pseudo-natural polymer with a positive charge (cationic) [142], which can interact with negatively-charged DNA, membranes of microbial cells, and biofilm matrix [143]. Antimicrobial studies with CUR in CS are summarized in Table 6.

36. Fernanda Alves; Gabriela Gomes Guimarães; Natália Mayumi Inada; Sebastião Pratavieira; Vanderlei Salvador Bagnato; Cristina Kurachi; Strategies to Improve the Antimicrobial Efficacy of Photodynamic, Sonodynamic, and Sonophotodynamic Therapies. *Lasers in Surgery and Medicine* 2021, null, 1-9, 10.1002/lsm.23383. Table 6. Antimicrobial studies performed with CUR in CS.

Type of CS	[CUR] Formulation	Microorganism	Type of Culture	Antimicrobial Method	Antimicrobial [CUR]	Reference
PEG-CS	4.4%, 5 mg/mL	MRSA, <i>P. aeruginosa</i>	Planktonic, Animal model	OD _{600nm} , CFU	5 and 10 mg/mL *	[144]

20043.

3	CCS microspheres	12.27 mg/mL, 1 mol	<i>S. aureus</i> , <i>E. coli</i>	Planktonic	Zone of inhibition, MIC	N/R	[145]	tiérrez-
	CS nanoparticles	1.06 mg/mL	<i>S. mutans</i>	Planktonic, Biofilm	MIC	0.114 mg/mL	[146]	olytic
3	CS-CMS-MMT	0.0004–0.004 g	<i>S. mutans</i>	Planktonic, Biofilm	MIC	0.101 mg/mL	[147]	2019, 9,
	CS-GP-CUR	148.09 ± 5.01 µg	<i>S. aureus</i>	Planktonic	Zone of inhibition, tissue bacteria count	N/C	[148]	n the
4	PVA-CS-CUR	N/C	<i>E. coli</i> , <i>P. aeruginosa</i> , <i>S. aureus</i> , <i>B. subtilis</i>	Planktonic	Zone of inhibition	N/R	[149]	2019,
	PVA-CS-CUR	10, 20, 30 mg	<i>P. multocida</i> , <i>S. aureus</i> , <i>E. coli</i> , <i>B. subtilis</i>	Planktonic	Zone of inhibition	10, 20, 30 mg	[150]	st
4	CS NPs	2, 4, 8, 16%	<i>C. albicans</i> , <i>S. aureus</i>	Planktonic, Biofilm	MIC, Colony count	400 mg/mL	[151]	02.
	CS NPs	4 mg/mL	HCV-4	N/R	Antiviral assay	15 µg/mL	[152]	ce the
4	CS/milk protein nanocomposites	100 mg	PVY	Plant infection	Antiviral activity	500, 1000, 1500 mg/100 mL	[153]	gy

Acinetobacter baumannii. *Rapid Communications in Mass Spectrometry* **2019**, 34, e8548, 10.1002/rcm.8548.

44. Javad Yasbolaghi Sharahi; Zahra Aliakbar Ahovan; Donya Taghizadeh Maleki; Zahra Riahi Rad; [CUR]: CUR concentration. N/R: not reported. N/C: not clear. *: formulation concentration. Zohreh Riahi Rad; Mehdi Goudarzi; Aref Shariati; Narjess Bostanghadiri; Elham Abbasi; Ali

3.7. CUR in Other Polymeric DDS

Hashemi et al. In vitro antibacterial activity of curcumin-meropenem combination against extensively drug-resistant (XDR) bacteria isolated from burn wound infections.. *Avicenna J Phytotherapy* **2020**, 10, 3–10.

Antimicrobial studies with CUR loaded in other polymeric DDSs are summarized in Table 7.

45. Jourdan E. Lakes; Christopher J. Richards; Michael D. Flythe; Inhibition of Bacteroidetes and Firmicutes by select phytochemicals. *Anaerobe* **2020**, 61, 102145-102145, 10.1016/j.anaerobe.20

Table 7. Antimicrobial studies performed with curcumin in polymeric drug delivery systems.

4	Type of Polymeric DDS	[CUR] Formulation	Microorganism	Type of Culture	Antimicrobial Method	Antimicrobial [CUR]	Light/Ultrasonic Parameters	Reference	ma;
	PEG 400γ-CD and PEG + β-CD	0.18%	<i>E. faecalis</i> , <i>E. coli</i>	Planktonic	CFU/mL aPDT	N/R	9.7 J/cm ² 29 J/cm ²	[154]	al class

Biology and Medicine **2019**, 143, 140-145, 10.1016/j.freeradbiomed.2019.08.003.

4	CUR-NP without polymer	100 mg	<i>S. aureus</i> , <i>B. subtilis</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>P. notatum</i> , <i>A. niger</i>	Planktonic	MIC Inhibition zone	100 mg, 0.27 mmol	-	[155]	andeep;
4	CUR-NP without polymer	100 mg	<i>M. luteus</i> , <i>S. aureus</i> , <i>E. coli</i> , <i>P. aeruginosa</i>	Planktonic	MBC	N/R	-	[156]	inal
	Mixed polymer NP	5 mM	<i>E. coli</i>	Planktonic	MIC	400–500 µM	-	[157]	ilarri;
	CTABTween 20Sodium dodecylsulfate	100 mg/mL	<i>L. monocytogenes</i>	Planktonic	Inhibition zone	N/R	-	[158]	ers; et of 3,3'-
4	PLA/dextran sulfate	4 mg/mL	MRSA, <i>C. albicans</i> , <i>S. mutans</i>	Planktonic/mono- and –mixed biofilm	aPDT	260 µM	43.2 J/cm ²	[159]	/ 2019,
	PLA/dextran sulfate	0.4%	<i>C. albicans</i>	Animal model	aPDT	260 µM	37.5 J/cm ²	[160]	s da
	Nanocurcumin	N/R	<i>P. aeruginosa</i> (isolates) and standard strain	Planktonic	MIC	128 µg/mL	-	[161]	a
5	PLGA	5 mg	<i>S. saprophyticus</i> subsp. <i>Bovis</i> , <i>E. coli</i>	Planktonic	aPDT	50 µg/mL	13.2 J/cm ²	[162]	et al.
	Eudragit L-100	N/C	<i>L. monocytogenes</i>	Planktonic	Animal model infection	N/R	-	[163]	2020.1
5	nCUR	N/R	<i>S. mutans</i>	PlanktonicBiofilm	Inhibition zoneaPDT	N/R	300–420 J/cm ²	[164]	ed
	nCUR combined with indocyanine	100 mg	<i>E. faecalis</i>	Biofilm	Metabolic activity	N/R	500 mW/cm ²	[165]	0.3390/
5	PVAc-CUR-PET-PVDC	0.02 g	<i>S. aureus</i> , <i>S. tiphimurium</i>	Planktonic	aPDT	N/R	24, 48, and 72 J/cm ²	[166]	a
	MOA.CUR-PLGA-NP	Up to 10%	<i>S. mutans</i>	Biofilm	aPDT	7% wt	45 J/cm ²	[167]	ador of
	CS- β-CD	N/C	<i>S. aureus</i> , <i>E. coli</i>	Planktonic	Colony count	Up to 0.03%	-	[168]	alysis. 34.

53. Sivadas Ganapathy; Shan Sainudeen; Veena S Nair; Mohammad Zarbah; Anshad Mohamed Abdulla; Chawre Mustufa Najeeb; Can herbal extracts serve as antibacterial root canal irrigating solutions? Antimicrobial efficacy of *Tylophora indica*, *Curcumin longa*, *Phyllanthus amarus*, and sodium hypochlorite on *Enterococcus faecalis* biofilms formed on tooth substrate: In vitro study. *Journal of Pharmacy And Bioallied Sciences* **2019**, 12, 423-S429, 10.4103/jpbs.jpbs_127_20.
54. Arash Azizi; Parastoo Shohrati; Mehdi Goudarzi; Shirin Lawaf; Arash Rahimi; Comparison of the effect of photodynamic therapy with curcumin and methylene Blue on streptococcus mutans bacterial colonies. *Photodiagnosis and Photodynamic Therapy* **2019**, 27, 203-209, 10.1016/j.pdpdt.2019.06.002.

55. Jennifer Machado Soares; Karoliny Oliveira Epinas Silva; Natalia Mayumi Inada; Vanderlei

Salvador Bagnato; Kate Cristina Blanco; Optimization for microbial incorporation and efficiency of
3.8. CUR with Metallic Nanoparticles

Photodynamic Therapy **2020**, 29, 101652, 10.1016/j.pdpdt.2020.101652.

Metal complexation plays an important role in the therapeutic properties of CUR. The β -diketone moiety in the CUR

56. Daniela Alejandra Gusciano; Méndez, Eliezer Gutierrez; Giuliana Campos Chaves Lamas; the

antimicrobial activity of CUR and Curcuminoid complexes with metals, such as Boron, Ca, Cu, Cu²⁺, Cu²⁺,

Fe³⁺, Fe²⁺, Mg²⁺, Ni²⁺, Pb²⁺, Pt²⁺, Zn²⁺, and Zn²⁺ against viruses, bacteria, and fungi. [169]

also been combined with polymers to improve the biological effects of CUR and go to be used as films, hydrogels,

dressing, and other pharmaceutical formulations. [170]

57. Xinlong Li, Luoping Yin, Gordon Ramage, Bingchun Li, Ye Tao, Qinghui Zhi, Huancai Lin, Yan

Zhou, Assessing the impact of curcumin on dual-species biofilms formed by *Streptococcus*

mutans and *Candida albicans*. *MicrobiologyOpen* **2019**, 8, e937, 10.1002/mbo3.937.

58. Marzie Mahdizade-Ari; Maryam Pourhajibagher; Abbas Bahador; Changes of microbial cell
 survival, metabolic activity, efflux capacity, and quorum sensing ability of *Aggregatibacter*
actinomycetemcomitans due to antimicrobial photodynamic therapy-induced bystander effects.
Photodiagnosis and Photodynamic Therapy **2019**, 26, 287-294, 10.1016/j.pdpdt.2019.04.021.

59. Hui Pan; Dongqing Wang; Fengqiu Zhang; In vitro antimicrobial effect of curcumin-based
 photodynamic therapy on *Porphyromonas gingivalis* and *Aggregatibacter*
actinomycetemcomitans. *Photodiagnosis and Photodynamic Therapy* **2020**, 32, 102055, 10.1016/
 j.pdpdt.2020.102055.

60. Sarah Böcher; Johannes-Simon Wenzler; Wolfgang Falk Andreas Braun; Comparison of different
 laser-based photochemical systems for periodontal treatment. *Photodiagnosis and Photodynamic*
Therapy **2019**, 27, 433-439, 10.1016/j.pdpdt.2019.06.009.

61. Lucas Henrique De Paula Zago; Sarah Raquel de Annunzio; Kleber Thiago de Oliveira; Paula
 Aboud Barbugli; Belen Retamal Valdes; Magda Feres; Carla Raquel Fontana; Antimicrobial
 photodynamic therapy against metronidazole-resistant dental plaque bacteria. *Journal of*
Photochemistry and Photobiology B: Biology **2020**, 209, 111903, 10.1016/j.jphotobiol.2020.11190

Figure 6. Schematic representation of CUR in silver nanoparticles.

Table 8. Antimicrobial studies performed with CUR complexes with metallic NPs.

Type of Metallic Material	[CUR] Formulation	Microorganism	Type of Culture	Antimicrobial Method	Antimicrobial [CUR]	Reference
CUR-AgNPs	20 mg/mL	<i>P. aeruginosa</i> , <i>E. coli</i> , <i>B. subtilis</i> , <i>S. aureus</i>	Planktonic	MIC	20 mg/mL	[173]
Ag-CUR-nanoconjugates	0.1 mM	<i>E. coli</i> , <i>Salmonella</i>	Planktonic	Zone of Inhibition	0.1 mM	[174]

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			spp., <i>Fusarium</i> spp., <i>S. aureus</i>					6/j.pdp
6	AgCURNPs	500 mg	<i>P. aeruginosa</i> , <i>S. aureus</i>	Biofilm	CLSM SEM	Up to 400 µg/mL	[175]	a
	AgNPs	7 mg	<i>E. coli</i>	Planktonic	Turbidimetric Assay	0.005 µM	[176]	gnato; IDS.
	cAgNPs	7 mg	<i>E. coli</i> , <i>B. subtilis</i>	Planktonic	MIC, CFU/mL	7 mg	[177]	774.
6	Ru II complex	0.092 g	<i>E. coli</i> , <i>S. aureus</i> , <i>K. pneumoniae</i> , <i>A. baumannii</i> , <i>P. aeruginosa</i> , <i>Enterococcus</i> sp.	Planktonic	MIC/FICI	>64 µg/mL	[178]	man e of jdr.IJD
6	SCMC SNCF nanocomposites with CUR	0.25 mg/mL	<i>E. coli</i>	Planktonic	Disc Method Count Method	2 mg/mL	[179]	efficacy biofilms 019,
6	CSCL CUR-AgNP	0.092 g	<i>E. coli</i> , <i>B. subtilis</i>	Planktonic	Zone of Inhibition	10 and 20 µM	[180]	raújo; De
	nSnH	10%	<i>S. aureus</i> , <i>E. coli</i>	Planktonic	CFU/mL	N/R	[181]	apy 26,
6	Nanocomposite of CUR and ZnO NPs	N/C	<i>S. epidermidis</i> , <i>S. hemolyticus</i> , <i>S. saprophyticus</i>	Planktonic	Zone of Inhibition	1000, 750, 500, 250 µg/mL	[182]	rapy amic
6	Thermo-responsive hydrogels	N/C	<i>S. aureus</i> , <i>P. aeruginosa</i> , <i>E. coli</i>	Planktonic	MIC	400 µg/mL	[183]	as; Ana ene 20, 31,
	CUR-AgNPs	5 mg/mL	<i>C. albicans</i> , <i>C. glabrata</i> , <i>C. tropicalis</i> , <i>C. parapsilosis</i> , <i>C. krusei</i> , <i>C. kefyr</i>	Planktonic	Zone of Inhibition, MIC	32.2–250 µg/mL	[184]	alena
7	Gel-CUR-Ag	20 mg	<i>P. aeruginosa</i> , <i>S. aureus</i>	Planktonic	MIC, MBC	20 mg	[185]	ER
	HGZ-CUR	N/C	<i>S. aureus</i> , <i>T. rubrum</i>	Planktonic	Zone of Inhibition	N/C	[186]	nrique
7	CHG-ZnO-CUR	N/C	<i>S. aureus</i> , <i>T. rubrum</i>	Planktonic	Zone of Inhibition	N/C	[187]	

Goldman; Ewerton Garcia De Oliveira Mima; Verapamil inhibits efflux pumps in *Candida albicans*, exhibits synergism with fluconazole, and increases survival of *Galleria mellonella*. *Virulence* **2020**, *12*, 231-243, 10.1080/21505594.2020.1868814.

7	Copper (II) oxide NPs	1 g	<i>E. faecalis</i> , <i>P. aeruginosa</i>	Planktonic	Zone of Inhibition CFU/mL	1 mg/mL	[188]	kash onyl and
7	OA-Ag-C	1 g	<i>P. aeruginosa</i> , <i>S. aureus</i>	Planktonic	OD _{600nm}	2.5 mg/mL	[189]	4.
7	Ag-NP-β-CD-BC	0.79 g	<i>P. aeruginosa</i> , <i>S. aureus</i> , <i>C. auris</i>	Planktonic	Zone of Inhibition	N/R	[190]	0.3390/
7	Cotton fabrics coated ZnO-NP	2.71×10^{-3} M	<i>S. aureus</i> , <i>E. coli</i>	Planktonic	Bacterial Count	N/R	[191]	7, 40,
7	CS-ZnO-CUR	0.2 g	<i>S. aureus</i> , <i>E. coli</i>	Planktonic	MIC, MBC	Up to 50 µg/mL	[192]	nds as
7	CUR-TiO ₂ -CS	100–300 mg	<i>S. aureus</i> , <i>E. coli</i>	Planktonic Animal infection	MIC	10 mg	[193]	ACE2
7	CUR-Au-NPs	1 mg/mL	<i>E. coli</i> , <i>B. subtilis</i> , <i>S. aureus</i> , <i>P. aeruginosa</i>	Planktonic	Zone of Inhibition	100, 200, 300 µg/mL	[194]	n.

77. Mohit Kumar, Rushmeet Kaur Sooni, Dheep Kumar Singh, Addressing the potential role of curcumin in the prevention of COVID-19 by targeting the Nsp9 replicase protein through molecular docking. *Archives of Microbiology* **2021**, 203, 1691-1696, 10.1007/s00203-020-02163-0 [CUR]: CUR concentration. N/R: not reported. N/C: not clear.

3.9. CUR in Mesoporous Particles

78. Ashish Patel; Malathi Rajendran; Ashish Shah; Harnisha Patel; Suresh B. Pakala; Prashanthi Karyala; Virtual screening of curcumin and its analogs against the spike surface glycoprotein of SARS-CoV-2 and SARS-CoV. *Journal of Biomolecular Structure and Dynamics*, **2021**, 5, 1-9, 10.1080/07391102220201868338

79. Loubna Allam; Fatima Ghri; Hakmi Mohammed; Naima El Hafidi; Rachid El Jaoudi; Jaouad El Harti; Badreddine Lmimouni; Lahcen Belyamani; Azeddine Ibrahimi; Targeting the GRP78-structure, large specific surface area, and versatile chemistry for functionalization [196]. Mesoporous materials can be synthesized using carbon, silica, and metal oxides [196]. Mesoporous silica nanoparticles (MSN, Figure 7) are inorganic scaffolds [197], which seemed ideal carriers for hydrophobic drugs due to their well-defined structure, large specific surface area, and versatile chemistry for functionalization [198]. The pore size and volume dependant SARS-CoV-2 Cell Entry by Peptides and Small Molecules. *Bioinformatics and Biology Insights* **2019**, 14, 1177932220965505, 10.1177/1177932220965505.

80. Mahmoud A. A. Ibrahim; Alaa H. M. Abdelrahman; Taha A. Hussien; Esraa A. A. Badr; Tarik A. Mohamed; Hesham R. El Seedi; Paul W. Pare; Thomas Efferth; Mohamed Elamir F. Hegazy; In-silico drug discovery of major metabolites from spices as SARS-CoV-2 main protease inhibitors. *Computers in Biology and Medicine* **2020**, 126, 104046-104046, 10.1016/j.compbimed.2020.104046.

81. Suresh Kumar; Priya Kashyap; Suman Chowdhury; Shivani Kumar; Anil Panwar; Ashok Kumar; Identification of phytochemicals as potential therapeutic agents that binds to Nsp15 protein target of coronavirus (SARS-CoV-2) that are capable of inhibiting virus replication. *Phytomedicine* **2021**, 85, 153317-153317, 10.1016/j.phymed.2020.153317.

82. Vimal K. Maurya; Swatantra Kumar; Anil K. Prasad; Madan L. B. Bhatt; Shailendra K. Saxena; Structure-based drug designing for potential antiviral activity of selected natural products from Ayurveda against SARS-CoV-2 spike glycoprotein and its cellular receptor. *VirusDisease* **2020**, 31, 179-193, 10.1007/s13337-020-00598-8.
83. Jiao Wang; Xiaoli Zhang; Alejandra B. Omarini; Binglin Li; Virtual screening for functional foods against the main protease of SARS-CoV-2. *Journal of Food Biochemistry* **2020**, 44, 13481, 10.1111/jfbc.13481.
84. Debmalya Barh; Sandeep Tiwari; Marianna E. Weener; Vasco Azevedo; Aristóteles Góes-Neto; M. Michael Gromiha; Presenting Author; Multi-omics-based identification of SARS-CoV-2 infection biology and candidate drugs against COVID-19. *Computers in Biology and Medicine* **2020**, 126, 104051-104051, 10.1016/j.compbiomed.2020.104051.

Table 9. Antimicrobial studies performed with CUR in porous DDSs.

Porous DDS	[CUR] Formulation	Microorganism	Type of Culture	Antimicrobial Method	Antimicrobial [CUR]	Light/Ultrasonic Parameters	Reference
Cu-SNP/Ag	1.0 mmol	<i>E. coli</i>	Planktonic	aPDT	N/R	72 J/cm ²	[200]
Bionanocomposite silica/chitosan	100 mg	<i>E. coli</i> , <i>S. aureus</i>	Planktonic	Zone of inhibition	N/R	-	[201]
NCIP	1 mg	HIV-1	Transfected cells	Immuno fluorescent staining	5–8 mg/mL	-	[202]
Lollipop-like MSN	30 mg L ⁻¹	<i>E. coli</i> , <i>S. aureus</i>	Planktonic	OD _{600nm}	N/R	-	[203]
SBA-15/PDA/Ag	2 mg	<i>E. coli</i> , <i>S. aureus</i>	Planktonic	CFU/mL	50 mM	-	[204]

John Francis Callan; Antimicrobial sonodynamic and photodynamic therapies against *Candida albicans*. *Biofouling* **2018**, 34, 357-367, 10.1080/08927014.2018.1439935.

89. Fatemeh Forouzanfar; Ali Forouzanfar; Thozhukat Sathyapalan; Hossein M. Orafi; Amirhossein Sahebkar; Curcumin for the Management of Periodontal Diseases: A Review. *Current Pharmaceutical Design* **2020**, 26, 4277-4284, 10.2174/1381612826666200513112607.

3.10. CUR in Quantum Dots

90. Kourosh Cheraghipour; Behrouz Ezatpour; Leila Masoori; Abdolrazagh Marzban; Asghar Sepahvand; Arian Karimi Rouzbahani; Abbas Moridnia; Sayyad Khanizadeh; Hossein Mahmoudvand; Anti-Candida Activity of Curcumin: A Systematic Review. *Current Drug Discovery Technologies* **2021**, 18, 379-390, 10.2174/1570163817666200518074629.
91. Kazumasa Ito; Akihiro Harada; Yukie Nagasaki; Block copolymer micelles for CUR delivery: design, characterization and biological significance. *Advanced Drug Delivery Reviews* **2001**, 47, 113-131, 10.1016/s0169-409x(00)00124-1.

Table 10. Antimicrobial studies performed with CUR in quantum dots (QDs).

92. Muhammad Usman Akbar; Khalid Mahmood Zia; Ahsan Nazir; Jamshed Iqbal; Syeda Abida Ejaz; Muhammad Sajid Hamid Akash; Pluronic-Based Mixed Polymeric Micelles Enhance the

Type of Material	[CUR] Formulation	Microorganism	Type of Culture	Antimicrobial Method	Antimicrobial [CUR]	Light/Ultrasonic Parameters	Reference	2249-0
CUR-cQDs	0.6	<i>S. aureus</i> MRSA <i>E. faecalis</i> <i>E. coli</i> <i>K. pneumoniae</i> <i>P. aeruginosa</i>	Planktonic Biofilm	Grown inhibition Biomass evaluation Confocal microscopy	3.91– 7.825 µg/mL	-	[206]	inquired cesami.
CUR-cQDs	200 mg	EV-71	Cell infection Animal infection	MIC Plaque assay TC IC50 assay Western blot PCR	5 µg/mL	-	[207]	n s11033
CUR-MQD	2:1 wt%	<i>K. pneumoniae</i> <i>P. aeruginosa</i> <i>S. aureus</i>	Planktonic	MIC MBC Confocal microscopy Fluorescence microscopy Flow cytometry	<0.00625– 0.125 µg/mL	-	[208]	ct in l.2017.
CUR-GQDs	N/C	A. actinomycetemcomitans <i>P. gingivalis</i> <i>P. intermedia</i>	Mixed biofilm	aPDT	100 µg/mL	60–80 J/cm ²	[209]	Email US

nanomicelle curcumin. *Photodiagnosis and Photodynamic Therapy* **2020**, 30, 101780, 10.1016/j.pdpdt.2020.101780.

97. Katia Rupel; Luisa Zupin; Silvia Brich; Mario Mardirossian; Giulia Ottaviani; Margherita Gobbo; Roberto Di Lenarda; Sabrina Pricl; Sergio Crovella; Serena Zacchigna; et al. Matteo Biasotto Antimicrobial activity of amphiphilic nanomicelles loaded with curcumin against *Pseudomonas aeruginosa* alone and activated by blue laser light. *Journal of Biophotonics* **2020**, 14, null, 10.1002/jbpo.202000350.
98. Victor Hugo Cortez Dias; Amanda Milene Malacrida; Adriele Rodrigues dos Santos; Andreia Farias Pereira Batista; Paula Aline Zanetti Campanerut-Sá; Gustavo Braga; Evandro Bona; Wilker Caetano; Jane Martha Graton Mikcha; pH interferes in photoinhibitory activity of curcumin nanoencapsulated with pluronic® P123 against *Staphylococcus aureus*. *Photodiagnosis and Photodynamic Therapy* **2021**, 33, 102085, 10.1016/j.pdpdt.2020.102085.
99. Yanhui Zhu; Qiaojie Luo; Hongjie Zhang; Qiuquan Cai; Xiaodong Li; Zhiquan Shen; Weipu Zhu; A shear-thinning electrostatic hydrogel with antibacterial activity by nanoengineering of polyelectrolytes. *Biomaterials Science* **2019**, 8, 1394-1404, 10.1039/c9bm01386e.
100. Caio H N Barros; Dishon W Hiebner; Stephanie Fulaz; Stefania Vitale; Laura Quinn; Eoin Casey; Synthesis and self-assembly of curcumin-modified amphiphilic polymeric micelles with antibacterial activity.. *Journal of Nanobiotechnology* **2021**, 19, 104.

101. N.P. Aditya; Geetanjali Chimote; Karthigayan Gunalan; Rinti Banerjee; Swati Patankar; Basavaraj Madhusudhan; Curcuminoids-loaded liposomes in combination with arteether protects against *Plasmodium berghei* infection in mice. *Experimental Parasitology* **2012**, 131, 292-299, 10.1016/j.exppara.2012.04.010.
102. Soumitra Shome; Anupam Das Talukdar; Manabendra Dutta Choudhury; Mrinal Kanti Bhattacharya; Hrishikesh Upadhyaya; Curcumin as potential therapeutic natural product: a nanobiotechnological perspective. *Journal of Pharmacy and Pharmacology* **2016**, 68, 1481-1500, 10.1111/jphp.12611.
103. Yan Chen; Yao Lu; Robert J Lee; Guangya Xiang; Nano Encapsulated Curcumin: And Its Potential for Biomedical Applications. *International Journal of Nanomedicine* **2020**, ume 15, 3099-3120, 10.2147/ijn.s210320.
104. Ting Ding; Tingting Li; Zhi Wang; Jianrong Li; Curcumin liposomes interfere with quorum sensing system of *Aeromonas sobria* and in silico analysis. *Scientific Reports* **2017**, 7, 1-16, 10.1038/s41598-017-08986-9.
105. Anuj Mittal; Naveen Kumar; Nar Singh Chauhan; Curcumin Encapsulated PEGylated Nanoliposomes: A Potential Anti-Infective Therapeutic Agent. *Indian Journal of Microbiology* **2019**, 59, 336-343, 10.1007/s12088-019-00811-3.
106. Sara Battista; Maria Anna Maggi; Pierangelo Bellio; Luciano Galantini; Angelo Antonio D'Archivio; Giuseppe Celenza; Roberta Colaiezzi; Luisa Giansanti; Curcuminoids-loaded liposomes: influence of lipid composition on their physicochemical properties and efficacy as delivery systems. *Colloids and Surfaces A: Physicochemical and Engineering Aspects* **2020**, 597, 124759, 10.1016/j.colsurfa.2020.124759.
107. Mengqian Gao; Xue Long; Jing Du; Mengting Teng; Weichen Zhang; Yuting Wang; Xingqi Wang; Ziyuan Wang; Peng Zhang; Jun Li; et al. Enhanced curcumin solubility and antibacterial activity by encapsulation in PLGA oily core nanocapsules. *Food & Function* **2019**, 11, 448-455, 10.1039/c9fo00901a.
108. Eshant Bhatia; Shivam Sharma; Kiran Jadhav; Rinti Banerjee; Combinatorial liposomes of berberine and curcumin inhibit biofilm formation and intracellular methicillin resistant *Staphylococcus aureus* infections and associated inflammation. *Journal of Materials Chemistry B* **2020**, 9, 864-875, 10.1039/d0tb02036b.
109. Heba A. Hazzah; Ragwa M. Farid; Maha M.A. Nasra; Walaa A. Hazzah; Magda A. El-Massik; Ossama Y. Abdallah; Gelucire-Based Nanoparticles for Curcumin Targeting to Oral Mucosa: Preparation, Characterization, and Antimicrobial Activity Assessment. *Journal of Pharmaceutical Sciences* **2015**, 104, 3913-3924, 10.1002/jps.24590.
110. Min Sun; Xun Su; Buyun Ding; Xiuli He; Xiuju Liu; Aihua Yu; Hongxiang Lou; Guangxi Zhai; Advances in nanotechnology-based delivery systems for curcumin. *Nanomedicine* **2012**, 7, 1085-

- 1100, 10.2217/nnm.12.80.
111. Ankur Gupta; Huseyin Burak Eral; Trevor Alan Hatton; Patrick S. Doyle; Nanoemulsions: formation, properties and applications. *Soft Matter* **2016**, *12*, 2826-2841, 10.1039/c5sm02958a.
 112. Gagan Flora; Deepesh Gupta; Archana Tiwari; Nanocurcumin: A Promising Therapeutic Advancement over Native Curcumin. *Critical Reviews in Therapeutic Drug Carrier Systems* **2012**, *30*, 331-368, 10.1615/critrevtherdrugcarriersyst.2013007236.
 113. Amit Mirani; Harish Kundaikar; Shilpa Velhal; Vainav Patel; Atmaram Bandivdekar; Mariam Degani; Vandana Patravale; Tetrahydrocurcumin-loaded vaginal nanomicrobicide for prophylaxis of HIV/AIDS: in silico study, formulation development, and in vitro evaluation. *Drug Delivery and Translational Research* **2019**, *9*, 828-847, 10.1007/s13346-019-00633-2.
 114. Caroline Measso Do Bonfim; Letícia Figueiredo Monteleoni; Marília De Freitas Calmon; Natália Maria Cândido; Paola Jocelan Scarin Provazzi; Vanesca De Souza Lino; Tatiana Rabachini; Laura Sichero; Luisa Lina Villa; Silvana Maria Quintana; et al. Patrícia Pereira Dos Santos Melli Fernando Lucas Primo Camila Amantino Antonio Tedesco Enrique Boccardo Paula Rahal Antiviral activity of curcumin-nanoemulsion associated with photodynamic therapy in vulvar cell lines transducing different variants of HPV-16. *Artificial Cells, Nanomedicine, and Biotechnology* **2019**, *48*, 515-524, 10.1080/21691401.2020.1725023.
 115. Najwa Nabila; Nadia Khansa Suada; Dionisius Denis; Benediktus Yohan; Annis Catur Adi; Anna Surgean Veterini; Atsarina Larasati Anindya; R. Tedjo Sasmono; Heni Rachmawati; Antiviral Action of Curcumin Encapsulated in Nanoemulsion against Four Serotypes of Dengue Virus. *Pharmaceutical Nanotechnology* **2020**, *8*, 54-62, 10.2174/2211738507666191210163408.
 116. Atinderpal Kaur; Yashaswee Saxena; Rakhi Bansal; Sonal Gupta; Amit Tyagi; Rakesh Kumar Sharma; Javed Ali; Amulya Kumar Panda; Reema Gabrani; Shweta Dang; et al. Intravaginal Delivery of Polyphenon 60 and Curcumin Nanoemulsion Gel.. *AAPS PharmSciTech* **2017**, *18*, 2188-2202, 10.1208/s12249-016-0652-6.
 117. Fahanwi Asabuwa Ngwabebhoh; Sevinc Ilkar Erdagi; Ufuk Yildiz; Pickering emulsions stabilized nanocellulosic-based nanoparticles for coumarin and curcumin nanoencapsulations: In vitro release, anticancer and antimicrobial activities. *Carbohydrate Polymers* **2018**, *201*, 317-328, 10.1016/j.carbpol.2018.08.079.
 118. Momin Khan, Muhammad Ali, Walayat Shah, Akram Shah & Muhammad Masoom Yasinzai; Curcumin-loaded self-emulsifying drug delivery system (cu-SEDDS): A promising approach for the control of primary pathogen and secondary bacterial infections in cutaneous leishmaniasis. *Applied Microbiology and Biotechnology volume* **2019**, *103*, 7481.
 119. Ayat F. Hashim; Said Hamed; Hoda A. Abdel Hamid; Kamel A. Abd-Elsalam; Iwona Golonka; Witold Musiał; Ibrahim M. El-Sherbiny; Antioxidant and antibacterial activities of omega-3 rich

- oils/curcumin nanoemulsions loaded in chitosan and alginate-based microbeads. *International Journal of Biological Macromolecules* **2019**, *140*, 682-696, 10.1016/j.ijbiomac.2019.08.085.
120. Kai Chen; Yong Qian; Senyi Wu; Xueqing Qiu; Dongjie Yang; Lei Lei; Neutral fabrication of UV-blocking and antioxidation lignin-stabilized high internal phase emulsion encapsulates for high efficient antibacterium of natural curcumin. *Food & Function* **2019**, *10*, 3543-3555, 10.1039/c9fo00320g.
 121. Agnieszka Lewińska; Anna Jaromin; Julia Jezierska; Role of architecture of N-oxide surfactants in the design of nanoemulsions for Candida skin infection. *Colloids and Surfaces B: Biointerfaces* **2020**, *187*, 110639, 10.1016/j.colsurfb.2019.110639.
 122. Jaya Lakkakula; Rui Werner Maçedo Krause; A vision for cyclodextrin nanoparticles in drug delivery systems and pharmaceutical applications. *Nanomedicine* **2014**, *9*, 877-894, 10.2217/nmm.14.41.
 123. Fliur Macaev; Veaceslav Boldescu; Athina Geronikaki; Natalia Sucman; Recent Advances in the Use of Cyclodextrins in Antifungal Formulations. *Current Topics in Medicinal Chemistry* **2013**, *13*, 2677-2683, 10.2174/15680266113136660194.
 124. Takuro Kurita; Yuji Makino; Novel curcumin oral delivery systems.. *Anticancer Research* **2013**, *33*, 2807–2821.
 125. E.M.Martin Del Valle; Cyclodextrins and their uses: a review. *Process Biochemistry* **2004**, *39*, 1033-1046, 10.1016/s0032-9592(03)00258-9.
 126. Atwood Jerry L.. *Comprehensive Supramolecular Chemistry*; Gokel George, Eds.; .: New York, USA, 1996; pp. 1.
 127. Phennapha Saokham; Chutimon Muankaew; Phatsawee Jansook; Thorsteinn Loftsson; Solubility of Cyclodextrins and Drug/Cyclodextrin Complexes. *Molecules* **2018**, *23*, 1161, 10.3390/molecules23051161.
 128. Mark E. Davis; Marcus E. Brewster; Cyclodextrin-based pharmaceuticals: past, present and future. *Nature Reviews Drug Discovery* **2004**, *3*, 1023-1035, 10.1038/nrd1576.
 129. Aaron J. Smith; John Oertle; Dino Prato; Multiple Actions of Curcumin Including Anticancer, Anti-Inflammatory, Antimicrobial and Enhancement via Cyclodextrin. *Journal of Cancer Therapy* **2014**, *06*, 257-272, 10.4236/jct.2015.63029.
 130. Anne Bee Hegge; Thorbjørn T. Nielsen; Kim L. Larsen; Ellen Bruzell; Hanne H. Tønnesen; Impact of Curcumin Supersaturation in Antibacterial Photodynamic Therapy—Effect of Cyclodextrin Type and Amount: Studies on Curcumin and Curcuminoides XLV. *Journal of Pharmaceutical Sciences* **2012**, *101*, 1524-1537, 10.1002/jps.23046.

131. Anne Bee Hegge; M. Vukicevic; E. Bruzell; S. Kristensen; H.H. Tønnesen; Solid dispersions for preparation of phototoxic supersaturated solutions for antimicrobial photodynamic therapy (aPDT). *European Journal of Pharmaceutics and Biopharmaceutics* **2012**, 83, 95-105, 10.1016/j.ejpb.2012.09.011.
132. Kristine Wikene; Anne Bee Hegge; Ellen Bruzell; Hanne Hjorth Tønnesen; Formulation and characterization of lyophilized curcumin solid dispersions for antimicrobial photodynamic therapy (aPDT): studies on curcumin and curcuminoids LII. *Drug Development and Industrial Pharmacy* **2014**, 41, 969-977, 10.3109/03639045.2014.919315.
133. Ilya Shlar; Samir Droby; Victor Rodov; Antimicrobial coatings on polyethylene terephthalate based on curcumin/cyclodextrin complex embedded in a multilayer polyelectrolyte architecture. *Colloids and Surfaces B: Biointerfaces* **2018**, 164, 379-387, 10.1016/j.colsurfb.2018.02.008.
134. A. Gupta; D.J. Keddie; V. Kannappan; H. Gibson; I.R. Khalil; M. Kowalczyk; C. Martin; X. Shuai; I. Radecka; Production and characterisation of bacterial cellulose hydrogels loaded with curcumin encapsulated in cyclodextrins as wound dressings. *European Polymer Journal* **2019**, 118, 437-450, 10.1016/j.eurpolymj.2019.06.018.
135. Shao-Pin Wang And Fu-Yung Huang Desu Naveen Kumar Reddy; Ramya Kumar; Shao-Pin Wang; Fu-Yung Huang; Curcumin-C3 Complexed with α -, β -cyclodextrin Exhibits Antibacterial and Antioxidant Properties Suitable for Cancer Treatments. *Current Drug Metabolism* **2020**, 20, 988-1001, 10.2174/1389200220666191001104834.
136. Nina Alizadeh; Shokufeh Malakzadeh; Antioxidant, antibacterial and anti-cancer activities of β - and γ -CDs/curcumin loaded in chitosan nanoparticles. *International Journal of Biological Macromolecules* **2020**, 147, 778-791, 10.1016/j.ijbiomac.2020.01.206.
137. Jochen Brasch; Vera Beck-Jendroschek; Grit Walther; Darian Rubbel; Clinical isolates of *Trichophyton rubrum* are completely inhibited by photochemical treatment with a γ -cyclodextrin formulation of curcuminoids. *Mycoses* **2020**, 63, 369-375, 10.1111/myc.13051.
138. Anna Stasiłowicz; Ewa Tykarska; Kornelia Lewandowska; Maciej Kozak; Andrzej Miklaszewski; Joanna Kobus-Cisowska; Daria Szymanowska; Tomasz Plech; Jacek Jencyk; Judyta Cielecka-Piontek; et al. Hydroxypropyl- β -cyclodextrin as an effective carrier of curcumin – piperine nutraceutical system with improved enzyme inhibition properties. *Journal of Enzyme Inhibition and Medicinal Chemistry* **2019**, 35, 1811-1821, 10.1080/14756366.2020.1801670.
139. Ilya Shlar; Samir Droby; Ruplal Choudhary; Victor Rodov; The mode of antimicrobial action of curcumin depends on the delivery system: monolithic nanoparticles vs. supramolecular inclusion complex. *RSC Advances* **2017**, 7, 42559-42569, 10.1039/c7ra07303h.
140. Mahsa Saheb; Narges Fereydouni; Saeideh Nemati; George E. Barreto; Thomas P. Johnston; Amirhossein Sahebkar; Chitosan-based delivery systems for curcumin: A review of

- pharmacodynamic and pharmacokinetic aspects. *Journal of Cellular Physiology* **2019**, 234, 12325-12340, 10.1002/jcp.28024.
141. Michelly Pellá; Michele K. Lima-Tenório; Ernandes Tenório-Neto; Marcos Rogério Guilherme; Edvani C. Muniz; Adley F. Rubira; Chitosan-based hydrogels: From preparation to biomedical applications. *Carbohydrate Polymers* **2018**, 196, 233-245, 10.1016/j.carbpol.2018.05.033.
 142. Marguerite Rinaudo; Chitin and chitosan: Properties and applications. *Progress in Polymer Science* **2006**, 31, 603-632, 10.1016/j.progpolymsci.2006.06.001.
 143. Ying-Chien Chung; Ya-Ping Su; Chiing-Chang Chen; Guang Jia; Huey-Lan Wang; J C Gaston Wu; Jaung-Geng Lin; Relationship between antibacterial activity of chitosan and surface characteristics of cell wall.. *Acta Pharmacologica Sinica* **2004**, 25, 932–936.
 144. Aimee E. Krausz; Brandon L. Adler; Vitor Cabral; Mahantesh Navati; Jessica Doerner; Rabab Charafeddine; Dinesh Chandra; Hongying Liang; Leslie Gunther; Alicea Clendaniel; et al.Stacey HarperJoel M. FriedmanJoshua D. NosanchukAdam J. Friedman Curcumin-encapsulated nanoparticles as innovative antimicrobial and wound healing agent. *Nanomedicine: Nanotechnology, Biology and Medicine* **2014**, 11, 195-206, 10.1016/j.nano.2014.09.004.
 145. T.S. Saranya; V.K. Rajan; Raja Biswas; R. Jayakumar; S. Sathianarayanan; Synthesis, characterisation and biomedical applications of curcumin conjugated chitosan microspheres. *International Journal of Biological Macromolecules* **2018**, 110, 227-233, 10.1016/j.ijbiomac.2017.12.044.
 146. Amir Maghsoudi; Fatemeh Yazdian; Saleheh Shahmoradi; Leila Ghaderi; Mehran Hemati; Ghassem Amoabediny; Curcumin-loaded polysaccharide nanoparticles: Optimization and anticariogenic activity against Streptococcus mutans. *Materials Science and Engineering: C* **2017**, 75, 1259-1267, 10.1016/j.msec.2017.03.032.
 147. Shabnam Jahanizadeh; Fatemeh Yazdian; Azam Marjani; Meisam Omid; Hamid Rashedi; Curcumin-loaded chitosan/carboxymethyl starch/montmorillonite bio-nanocomposite for reduction of dental bacterial biofilm formation. *International Journal of Biological Macromolecules* **2017**, 105, 757-763, 10.1016/j.ijbiomac.2017.07.101.
 148. Yong Zhao; Jia-Guo Liu; Wei-Min Chen; Ai-Xi Yu; Efficacy of thermosensitive chitosan/ β -glycerophosphate hydrogel loaded with β -cyclodextrin-curcumin for the treatment of cutaneous wound infection in rats. *Experimental and Therapeutic Medicine* **2017**, 15, 1304-1313, 10.3892/etm.2017.5552.
 149. Niranjana R.; Kaushik M.; Prakash J.; Venkataprasanna K.S.; Christy Arpana; Pannarselvam Balashanmugam; G. Devanand Venkatasubbu; Enhanced wound healing by PVA/Chitosan/Curcumin patches: In vitro and in vivo study. *Colloids and Surfaces B: Biointerfaces* **2019**, 182, 110339, 10.1016/j.colsurfb.2019.06.068.

150. Mazhar Abbas; Tariq Hussain; Muhammad Arshad; Abdur Rahman Ansari; Asma Irshad; Jan Nisar; Fida Hussain; Nasir Masood; Arif Nazir; Munawar Iqbal; et al. Wound healing potential of curcumin cross-linked chitosan/polyvinyl alcohol. *International Journal of Biological Macromolecules* **2019**, *140*, 871-876, 10.1016/j.ijbiomac.2019.08.153.
151. Su Ma; Doris Moser; Feng Han; Matthias Leonhard; Berit Schneider-Stickler; Yulong Tan; Preparation and antibiofilm studies of curcumin loaded chitosan nanoparticles against polymicrobial biofilms of *Candida albicans* and *Staphylococcus aureus*. *Carbohydrate Polymers* **2020**, *241*, 116254, 10.1016/j.carbpol.2020.116254.
152. Samah A Loutfy; Mostafa H Elberry; Khaled Yehia Farroh; Hossam Taha Mohamed; Aya A Mohamed; ElChaimaa B Mohamed; Ahmed Hassan Ibrahim Faraag; Shaker A Mousa; Antiviral Activity of Chitosan Nanoparticles Encapsulating Curcumin Against Hepatitis C Virus Genotype 4a in Human Hepatoma Cell Lines. *International Journal of Nanomedicine* **2020**, *ume 15*, 2699-2715, 10.2147/IJN.S241702.
153. Soad Hassan Taha; Ibrahim Mohamed El-Sherbiny; Aida Soliman Salem; Mahmoud Abdel-Hamid; Ali Hussein Hamed; Ghada Abady Ahmed; Antiviral Activity of Curcumin Loaded Milk Proteins Nanoparticles on Potato Virus Y. *Pakistan Journal of Biological Sciences* **2019**, *22*, 614-622, 10.3923/pjbs.2019.614.622.
154. Anne Bee Hegge; T. Andersen; J.E. Melvik; E. Bruzell; S. Kristensen; H.H. Tønnesen; Formulation and Bacterial Phototoxicity of Curcumin Loaded Alginate Foams for Wound Treatment Applications: Studies on Curcumin and Curcuminoides XLII. *Journal of Pharmaceutical Sciences* **2010**, *100*, 174-185, 10.1002/jps.22263.
155. Bhawana; Rupesh Kumar Basniwal; Harpreet Singh Buttar; V. K. Jain; Nidhi Jain; Curcumin Nanoparticles: Preparation, Characterization, and Antimicrobial Study. *Journal of Agricultural and Food Chemistry* **2011**, *59*, 2056-2061, 10.1021/jf104402t.
156. Mo'Ath Ahmad Adahoun; M-Ali Al-Akhras; Mohamad Suhaimi Jaafar; Mohamed Bououdina; Enhanced anti-cancer and antimicrobial activities of curcumin nanoparticles. *Artificial Cells, Nanomedicine, and Biotechnology* **2016**, *45*, 98-107, 10.3109/21691401.2015.1129628.
157. Ilya Shlar; Elena Poverenov; Yakov Vinokur; Batia Horev; Samir Droby; Victor Rodov; High-Throughput Screening of Nanoparticle-Stabilizing Ligands: Application to Preparing Antimicrobial Curcumin Nanoparticles by Antisolvent Precipitation. *Nano-Micro Letters* **2014**, *7*, 68-79, 10.1007/s40820-014-0020-6.
158. Da Som No; Ammar AlGhuri; Phong Huynh; Aubry Moret; Marion Ringard; Nicole Comito; Djamel Drider; Paul Takhistov; Michael L. Chikindas; Antimicrobial efficacy of curcumin nanoparticles against *Listeria monocytogenes* is mediated by surface charge. *Journal of Food Safety* **2017**, *37*, e12353, 10.1111/jfs.12353.

159. Jeffersson Krishan Trigo Gutierrez; Gabriela Cristina Zanatta; Ana Laura Mira Ortega; Maria Isabella Cuba Balastegui; Paula Volpato Sanitá; Ana Cláudia Pavarina; Paula Barbugli; Ewerton Garcia De Oliveira Mima; Encapsulation of curcumin in polymeric nanoparticles for antimicrobial Photodynamic Therapy. *PLOS ONE* **2017**, 12, e0187418, 10.1371/journal.pone.0187418.
160. Vinicius Tatsuyuji Sakima; Paula Aboud Barbugli; Paulo Sérgio Cerri; Marlus Chorilli; Juliana Cabrini Carmello; Ana Cláudia Pavarina; Ewerton Garcia De Oliveira Mima; Antimicrobial Photodynamic Therapy Mediated by Curcumin-Loaded Polymeric Nanoparticles in a Murine Model of Oral Candidiasis. *Molecules* **2018**, 23, 2075, 10.3390/molecules23082075.
161. Aref Shariati; Elham Asadian; Fatemeh Fallah; Taher Azimi; Ali Hashemi; Javad Yasbolaghi Sharahi; Majid Taati Moghadam; Evaluation of Nano-curcumin effects on expression levels of virulence genes and biofilm production of multidrug-resistant *Pseudomonas aeruginosa* isolated from burn wound infection in Tehran, Iran. *Infection and Drug Resistance* **2019**, ume 12, 2223-2235, 10.2147/idr.s213200.
162. Eduard Preis; Elias Baghdan; Michael R. Agel; Thomas Anders; Marcel Pourasghar; Marc Schneider; Udo Bakowsky; Spray dried curcumin loaded nanoparticles for antimicrobial photodynamic therapy. *European Journal of Pharmaceutics and Biopharmaceutics* **2019**, 142, 531-539, 10.1016/j.ejpb.2019.07.023.
163. Antonise M. Jaguezeski; Carine F. Souza; Gessica Perin; João H. Reis; Teane M.A. Gomes; Matheus Dellaméa Baldissera; Rodrigo A. Vaucher; Cinthia M. de Andrade; Lenita M. Stefani; Samanta Gündel; et al.Aline OuriqueAleksandro S. Da Silva Effect of free and nano-encapsulated curcumin on treatment and energetic metabolism of gerbils infected by *Listeria monocytogenes*. *Microbial Pathogenesis* **2019**, 134, 103564, 10.1016/j.micpath.2019.103564.
164. Maryam Pourhajibagher; Ladan Ranjbar Omrani; Mohammad Noroozian; Zahra Ghorbanzadeh; Abbas Bahador; In vitro antibacterial activity and durability of a nano-curcumin-containing pulp capping agent combined with antimicrobial photodynamic therapy. *Photodiagnosis and Photodynamic Therapy* **2021**, 33, 102150, 10.1016/j.pdpdt.2020.102150.
165. Maryam Pourhajibagher; Gianluca Plotino; Nasim Chiniforush; Abbas Bahador; Dual wavelength irradiation antimicrobial photodynamic therapy using indocyanine green and metformin doped with nano-curcumin as an efficient adjunctive endodontic treatment modality. *Photodiagnosis and Photodynamic Therapy* **2020**, 29, 101628, 10.1016/j.pdpdt.2019.101628.
166. Liwei Chen; Ziyue Song; Xiujuan Zhi; Bin Du; Photoinduced Antimicrobial Activity of Curcumin-Containing Coatings: Molecular Interaction, Stability and Potential Application in Food Decontamination. *ACS Omega* **2020**, 5, 31044-31054, 10.1021/acsomega.0c04065.
167. Hanie Ahmadi; Vahid Haddadi-Asl; Hassan-Ali Ghafari; Roghayeh Ghorbanzadeh; Yasaman Mazlum; Abbas Bahador; Shear bond strength, adhesive remnant index, and anti-biofilm effects of a photoexcited modified orthodontic adhesive containing curcumin doped poly lactic-co-glycolic

- acid nanoparticles: An ex-vivo biofilm model of *S. mutans* on the enamel slab bonded brackets. *Photodiagnosis and Photodynamic Therapy* **2020**, 30, 101674, 10.1016/j.pdpdt.2020.101674.
168. Kitipong Kiti; Orawan Suwantong; The potential use of curcumin- β -cyclodextrin inclusion complex/chitosan-loaded cellulose sponges for the treatment of chronic wound. *International Journal of Biological Macromolecules* **2020**, 164, 3250-3258, 10.1016/j.ijbiomac.2020.08.190.
 169. Abolfazl Shakeri; Yunes Panahi; Thomas P. Johnston; Amirhossein Sahebkar; Biological properties of metal complexes of curcumin. *BioFactors* **2019**, 45, 304-317, 10.1002/biof.1504.
 170. S.K. Bajpai; Sonam Ahuja; N. Chand; M. Bajpai; Nano cellulose dispersed chitosan film with Ag NPs/Curcumin: An in vivo study on Albino Rats for wound dressing. *International Journal of Biological Macromolecules* **2017**, 104, 1012-1019, 10.1016/j.ijbiomac.2017.06.096.
 171. Camila Fabiano de Freitas; Elza Kimura; Adley Forti Rubira; Edvani Curti Muniz; Curcumin and silver nanoparticles carried out from polysaccharide-based hydrogels improved the photodynamic properties of curcumin through metal-enhanced singlet oxygen effect. *Materials Science and Engineering: C* **2020**, 112, 110853, 10.1016/j.msec.2020.110853.
 172. Nelson Durán; Marcela Durán; Marcelo Bispo de Jesus; Amedea B. Seabra; Wagner Fávaro; Gerson Nakazato; Silver nanoparticles: A new view on mechanistic aspects on antimicrobial activity. *Nanomedicine: Nanotechnology, Biology and Medicine* **2016**, 12, 789-799, 10.1016/j.nano.2015.11.016.
 173. Swati Jaiswal; Prashant Mishra; Antimicrobial and antibiofilm activity of curcumin-silver nanoparticles with improved stability and selective toxicity to bacteria over mammalian cells. *Medical Microbiology and Immunology* **2017**, 207, 39-53, 10.1007/s00430-017-0525-y.
 174. Elsy El Khoury; Mohamad Abiad; Zeina G. Kassaify; Digambara Patra; Green synthesis of curcumin conjugated nanosilver for the applications in nucleic acid sensing and anti-bacterial activity. *Colloids and Surfaces B: Biointerfaces* **2015**, 127, 274-280, 10.1016/j.colsurfb.2015.01.050.
 175. Judy Ching Yee Loo; Ramin Rohanizadeh; Paul Young; Daniela Traini; Rosalia Cavaliere; Cynthia Whitchurch; Wing Hin Lee; Combination of Silver Nanoparticles and Curcumin Nanoparticles for Enhanced Anti-biofilm Activities. *Journal of Agricultural and Food Chemistry* **2015**, 64, 2513-2522, 10.1021/acs.jafc.5b04559.
 176. Ahmed M Abdellah; Mahmoud A Sliem; Mona Bakr†; Rehab M Amin; Green synthesis and biological activity of silver–curcumin nanoconjugates. *Future Medicinal Chemistry* **2018**, 10, 2577-2588, 10.4155/fmc-2018-0152.
 177. Zhiyong Song; Yang Wu; Huajuan Wang; Heyou Han; Synergistic antibacterial effects of curcumin modified silver nanoparticles through ROS-mediated pathways. *Materials Science and Engineering: C* **2019**, 99, 255-263, 10.1016/j.msec.2018.12.053.

178. Payal Srivastava; Manjulika Shukla; Grace Kaul; Sidharth Chopra; Ashis K. Patra; Rationally designed curcumin based ruthenium(ii) antimicrobials effective against drug-resistant *Staphylococcus aureus*. *Dalton Transactions* **2019**, 48, 11822-11828, 10.1039/c9dt01650c.
179. K. Varaprasad; K. Vimala; S. Ravindra; N. Narayana Reddy; G. Venkata Subba Reddy; K. Mohana Raju; Fabrication of silver nanocomposite films impregnated with curcumin for superior antibacterial applications. *Journal of Materials Science: Materials in Medicine* **2011**, 22, 1863-1872, 10.1007/s10856-011-4369-5.
180. Kunnavakkam Vinjimur Srivatsan; N. Duraipandy; Shajitha Begum; Rachita Lakra; Usha Ramamurthy; Purna Sai Korrapati; Manikantan Syamala Kiran; Effect of curcumin caged silver nanoparticle on collagen stabilization for biomedical applications. *International Journal of Biological Macromolecules* **2015**, 75, 306-315, 10.1016/j.ijbiomac.2015.01.050.
181. Sadiya Anjum; Amlan Gupta; Deepika Sharma; Deepti Gautam; Surya Bhan; Anupama Sharma; Arti Kapil; Bhuvanesh Gupta; Development of novel wound care systems based on nanosilver nanohydrogels of polymethacrylic acid with Aloe vera and curcumin. *Materials Science and Engineering: C* **2016**, 64, 157-166, 10.1016/j.msec.2016.03.069.
182. K. R. Soumya; S. Snigdha; Sheela Sugathan; Jyothis Mathew; E. K. Radhakrishnan; Zinc oxide–curcumin nanocomposite loaded collagen membrane as an effective material against methicillin-resistant coagulase-negative *Staphylococci*. *3 Biotech* **2017**, 7, 238, 10.1007/s13205-017-0861-z.
183. Thais Alves; Marco Chaud; Denise Grotto; Angela Faustino Jozala; Raksha Pandit; Mahendra Rai; Carolina Alves Dos Santos; Association of Silver Nanoparticles and Curcumin Solid Dispersion: Antimicrobial and Antioxidant Properties. *AAPS PharmSciTech* **2017**, 19, 225-231, 10.1208/s12249-017-0832-z.
184. Sony Paul; Kalyani Mohanram; Iyanar Kannan; Antifungal activity of curcumin-silver nanoparticles against fluconazole-resistant clinical isolates of *Candida* species. *AYU (An international quarterly journal of research in Ayurveda)* **2017**, 39, 182-186, 10.4103/ayu.ayu_24_18.
185. Ly Loan Khanh; Nguyen Thanh Truc; Nguyen Tan Dat; Nguyen Thi Phuong Nghi; Vo van Toi; Nguyen Thi Thu Hoai; Tran Ngoc Quyen; Tran Thi Thanh Loan; Nguyen Thi Hiep; Gelatin-stabilized composites of silver nanoparticles and curcumin: characterization, antibacterial and antioxidant study. *Science and Technology of Advanced Materials* **2019**, 20, 276-290, 10.1080/14686996.2019.1585131.
186. B. Anagha; Dhanya George; P. Uma Maheswari; K. M. Meera Sheriffa Begum; Biomass Derived Antimicrobial Hybrid Cellulose Hydrogel with Green ZnO Nanoparticles for Curcumin Delivery and its Kinetic Modelling. *Journal of Polymers and the Environment* **2019**, 27, 2054-2067, 10.1007/s10924-019-01495-y.
187. Dhanya George; Palanisamy Uma Maheswari; Khadar Mohamed Meera Sheriffa Begum; Gangasalam Arthanareeswaran; G Arthanaresswarn; Biomass-Derived Dialdehyde Cellulose

- Cross-linked Chitosan-Based Nanocomposite Hydrogel with Phytosynthesized Zinc Oxide Nanoparticles for Enhanced Curcumin Delivery and Bioactivity. *Journal of Agricultural and Food Chemistry* **2019**, 67, 10880-10890, 10.1021/acs.jafc.9b01933.
188. Shabnam Farkhonde Masoule; Maryam Pourhajibagher; Javad Safari; Mehdi Khoobi; Base-free green synthesis of copper(II) oxide nanoparticles using highly cross-linked poly(curcumin) nanospheres: synergistically improved antimicrobial activity. *Research on Chemical Intermediates* **2019**, 45, 4449-4462, 10.1007/s11164-019-03841-0.
 189. Yongbo Lyu; Mengchao Yu; Qisong Liu; Qingmei Zhang; Zhanhong Liu; Ye Tian; Defu Li; Mu Changdao; Synthesis of silver nanoparticles using oxidized amylose and combination with curcumin for enhanced antibacterial activity. *Carbohydrate Polymers* **2020**, 230, 115573, 10.1016/j.carbpol.2019.115573.
 190. Abhishek Gupta; Sophie Marie Briffa; Sam Swingler; Hazel Gibson; Vinodh Kannappan; Grazyna Adamus; Marek M. Kowalczyk; Claire Martin; Iza Radecka; Synthesis of Silver Nanoparticles Using Curcumin-Cyclodextrins Loaded into Bacterial Cellulose-Based Hydrogels for Wound Dressing Applications. *Biomacromolecules* **2020**, 21, 1802-1811, 10.1021/acs.biomac.9b01724.
 191. Issa M. El-Nahhal; Jamil Salem; Rawan Anbar; Fawzi S. Kodeh; Abdelraouf Elmanama; Preparation and antimicrobial activity of ZnO-NPs coated cotton/starch and their functionalized ZnO-Ag/cotton and Zn(II) curcumin/cotton materials. *Scientific Reports* **2020**, 10, 1-10, 10.1038/s41598-020-61306-6.
 192. Seyed-Behnam Ghaffari; Mohammad-Hossein Sarrafzadeh; Maryam Salami; M.Reza Khorramizadeh; A pH-sensitive delivery system based on N-succinyl chitosan-ZnO nanoparticles for improving antibacterial and anticancer activities of curcumin. *International Journal of Biological Macromolecules* **2020**, 151, 428-440, 10.1016/j.ijbiomac.2020.02.141.
 193. Roopesh Marulasiddeshwara; M.S. Jyothi; Khantong Soontarapa; Rangappa S. Keri; Rajendran Velmurugan; Nonwoven fabric supported, chitosan membrane anchored with curcumin/TiO₂ complex: Scaffolds for MRSA infected wound skin reconstruction. *International Journal of Biological Macromolecules* **2020**, 144, 85-93, 10.1016/j.ijbiomac.2019.12.077.
 194. N. Muniyappan; M. Pandeewaran; Augustine Amalraj; Green synthesis of gold nanoparticles using *Curcuma pseudomontana* isolated curcumin: Its characterization, antimicrobial, antioxidant and anti-inflammatory activities. *Environmental Chemistry and Ecotoxicology* **2020**, 3, 117-124, 10.1016/j.enceco.2021.01.002.
 195. Mark E. Davis; Ordered porous materials for emerging applications. *Nature* **2002**, 417, 813-821, 10.1038/nature00785.
 196. Xiao-Yu Yang; Li-Hua Chen; Yu Li; Joanna Claire Rooke; Clément Sanchez; Bao-Lian Su; Hierarchically porous materials: synthesis strategies and structure design. *Chemical Society Reviews* **2016**, 46, 481-558, 10.1039/c6cs00829a.

197. Alessandro Agostini; Félix Sancenón; Ramón Martínez-Máñez; María D. Marcos; Juan Soto; Pedro Amorós; A Photoactivated Molecular Gate. *Chemistry – A European Journal* **2012**, *18*, 12218-12221, 10.1002/chem.201201127.
198. Ying Wang; Qinfu Zhao; Ning Han; Ling Bai; Jia Li; Erxi Che; Liang Hu; Qiang Zhang; Tongying Jiang; Siling Wang; et al. Mesoporous silica nanoparticles in drug delivery and biomedical applications. *Nanomedicine: Nanotechnology, Biology and Medicine* **2015**, *11*, 313-327, 10.1016/j.nano.2014.09.014.
199. María Vallet-Regí; Francisco Balas; Daniel Arcos; Mesoporous Materials for Drug Delivery. *Angewandte Chemie International Edition* **2007**, *46*, 7548-7558, 10.1002/anie.200604488.
200. Yaswanth Kuthati; Ranjith Kumar Kankala; Prabhakar Busa; Shi-Xiang Lin; Jin-Pei Deng; Chung-Yuan Mou; Chia-Hung Lee; Phototherapeutic spectrum expansion through synergistic effect of mesoporous silica trio-nanohybrids against antibiotic-resistant gram-negative bacterium. *Journal of Photochemistry and Photobiology B: Biology* **2017**, *169*, 124-133, 10.1016/j.jphotobiol.2017.03.003.
201. Chunhua Wu; Yang Zhu; Tiantian Wu; Lin Wang; Yi Yuan; Jicheng Chen; Yaqin Hu; Jie Pang; Enhanced functional properties of biopolymer film incorporated with curcumin-loaded mesoporous silica nanoparticles for food packaging. *Food Chemistry* **2019**, *288*, 139-145, 10.1016/j.foodchem.2019.03.010.
202. Anu Sharma; Anita Yadav; Nikesh Gupta; Sandeep Sharma; Rita Kakkar; Katherine Cwiklinski; Elizabeth Quaye; Supriya D. Mahajan; Stanley A. Schwartz; Rakesh Kumar Sharma; et al. Multifunctional mesoporous curcumin encapsulated iron-phenanthroline nanocluster: A new Anti-HIV agent. *Colloids and Surfaces B: Biointerfaces* **2019**, *180*, 289-297, 10.1016/j.colsurfb.2019.04.057.
203. Yajun Cheng; Yudi Zhang; Weijun Deng; Jing Hu; Antibacterial and anticancer activities of asymmetric lollipop-like mesoporous silica nanoparticles loaded with curcumin and gentamicin sulfate. *Colloids and Surfaces B: Biointerfaces* **2020**, *186*, 110744, 10.1016/j.colsurfb.2019.110744.
204. Yiyang Song; Ling Cai; Zhongcheng Tian; Yuan Wu; Jin Chen; Phytochemical Curcumin-Coformulated, Silver-Decorated Melanin-like Polydopamine/Mesoporous Silica Composites with Improved Antibacterial and Chemotherapeutic Effects against Drug-Resistant Cancer Cells. *ACS Omega* **2020**, *5*, 15083-15094, 10.1021/acsomega.0c00912.
205. Siavash Iravani; Rajender S. Varma; Green synthesis, biomedical and biotechnological applications of carbon and graphene quantum dots. A review. *Environmental Chemistry Letters* **2020**, *18*, 703-727, 10.1007/s10311-020-00984-0.
206. Ashish Singh; Pradyot Prakash; Ranjana Singh; Nabarun Nandy; Zeba Firdaus; Monika Bansal; Ranjan K. Singh; Anchal Srivastava; Jagat K. Roy; Brahmeshwar Mishra; et al. Rakesh K. Singh

- Curcumin Quantum Dots Mediated Degradation of Bacterial Biofilms. *Frontiers in Microbiology* **2017**, 8, 1517, 10.3389/fmicb.2017.01517.
207. Chin-Jung Lin; Lung Chang; Han-Wei Chu; Han-Jia Lin; Pei-Ching Chang; Robert Y. L. Wang; Binesh Unnikrishnan; Ju-Yi Mao; Shiow-Yi Chen; Chih-Ching Huang; et al. High Amplification of the Antiviral Activity of Curcumin through Transformation into Carbon Quantum Dots. *Small* **2019**, 15, e1902641, 10.1002/smll.201902641.
 208. Ashish Kumar Singh; Himanshu Mishra; Zeba Firdaus; Shivangi Yadav; Prerana Aditi; Nabarun Nandy; Kavyanjali Sharma; Priyanka Bose; Akhilesh Kumar Pandey; Brijesh Singh Chauhan; et al. Kaushik Neogi; Kunwar Vikram Anchal; Srivastava Amrita; Ghosh Kar Pradyot; Prakash MoS2-Modified Curcumin Nanostructures: The Novel Theranostic Hybrid Having Potent Antibacterial and Antibiofilm Activities against Multidrug-Resistant Hypervirulent *Klebsiella pneumoniae*. *Chemical Research in Toxicology* **2019**, 32, 1599-1618, 10.1021/acs.chemrestox.9b00135.
 209. Maryam Pourhajibagher; Steven Parker; Nasim Chiniforush; Abbas Bahador; Photoexcitation triggering via semiconductor Graphene Quantum Dots by photochemical doping with Curcumin versus perio-pathogens mixed biofilms. *Photodiagnosis and Photodynamic Therapy* **2019**, 28, 125-131, 10.1016/j.pdpdt.2019.08.025.
 210. Mahtab Mirzahasseinipour; Khatereh Khorsandi; Reza Hosseinzadeh; Mehrgan Ghazaeian; Fedora Khatibi Shahidi; Antimicrobial photodynamic and wound healing activity of curcumin encapsulated in silica nanoparticles. *Photodiagnosis and Photodynamic Therapy* **2020**, 29, 101639, 10.1016/j.pdpdt.2019.101639.
 211. Gölnur Fakhrullina; Elvira Khakimova; Farida Akhatova; Giuseppe Lazzara; Filippo Parisi; Rawil F. Fakhrullin; Selective Antimicrobial Effects of Curcumin@Halloysite Nanoformulation: A *Caenorhabditis elegans* Study. *ACS Applied Materials & Interfaces* **2019**, 11, 23050-23064, 10.1021/acsami.9b07499.
 212. Xue Zou; Meng Yuan; Tongyu Zhang; Hongxia Wei; Shijie Xu; Na Jiang; Nan Zheng; Zhiwei Wu; Extracellular vesicles expressing a single-chain variable fragment of an HIV-1 specific antibody selectively target Env+ tissues. *Theranostics* **2018**, 9, 5657-5671, 10.7150/thno.33925.
 213. Julian M. Sotomil; Eliseu A. Münchow; Divya Pankajakshan; Kenneth J. Spolnik; Jessica A. Ferreira; Richard L. Gregory; Marco C. Bottino; Curcumin—A Natural Medicament for Root Canal Disinfection: Effects of Irrigation, Drug Release, and Photoactivation. *Journal of Endodontics* **2019**, 45, 1371-1377, 10.1016/j.joen.2019.08.004.
 214. Shabnam Sattari; Abbas Dadkhah Tehrani; Mohsen Adeli; Khadijeh Soleimani; Marzieh Rashidipour; Fabrication of new generation of co-delivery systems based on graphene-g-cyclodextrin/chitosan nanofiber. *International Journal of Biological Macromolecules* **2020**, 156, 1126-1134, 10.1016/j.ijbiomac.2019.11.144.

215. Yu-Ning Yang; Kun-Ying Lu; Pan Wang; Yi-Cheng Ho; Min-Lang Tsai; Fwu-Long Mi; Development of bacterial cellulose/chitin multi-nanofibers based smart films containing natural active microspheres and nanoparticles formed in situ. *Carbohydrate Polymers* **2020**, 228, 115370, 10.1016/j.carbpol.2019.115370.
216. Elaheh Esmaeili; Tarlan Eslami-Arshaghi; Simzar Hosseinzadeh; Elnaz Elahirad; Zahra Jamalpoor; Shadie Hatamie; Masoud Soleimani; The biomedical potential of cellulose acetate/polyurethane nanofibrous mats containing reduced graphene oxide/silver nanocomposites and curcumin: Antimicrobial performance and cutaneous wound healing. *International Journal of Biological Macromolecules* **2020**, 152, 418-427, 10.1016/j.ijbiomac.2020.02.295.
217. Yuewei Xi; Juan Ge; Min Wang; Mi Chen; Wen Niu; Wei Cheng; Yumeng Xue; Cai Lin; Bo Lei; Bioactive Anti-inflammatory, Antibacterial, Antioxidative Silicon-Based Nanofibrous Dressing Enables Cutaneous Tumor Photothermo-Chemo Therapy and Infection-Induced Wound Healing. *ACS Nano* **2020**, 14, 2904-2916, 10.1021/acsnano.9b07173.
218. Ali Shababdoust; Mojgan Zandi; Morteza Ehsani; Parvin Shokrollahi; Reza Foudazi; Controlled curcumin release from nanofibers based on amphiphilic-block segmented polyurethanes. *International Journal of Pharmaceutics* **2020**, 575, 118947, 10.1016/j.ijpharm.2019.118947.
219. Mengmeng Zhang; Bo Zhuang; Gangjun Du; Guang Han; Yiguang Jin; Curcumin solid dispersion-loaded in situ hydrogels for local treatment of injured vaginal bacterial infection and improvement of vaginal wound healing. *Journal of Pharmacy and Pharmacology* **2019**, 71, 1044-1054, 10.1111/jphp.13088.
220. Swarup Roy; Jong-Whan Rhim; Preparation of antimicrobial and antioxidant gelatin/curcumin composite films for active food packaging application. *Colloids and Surfaces B: Biointerfaces* **2020**, 188, 110761, 10.1016/j.colsurfb.2019.110761.
221. Swarup Roy; Jong-Whan Rhim; Carboxymethyl cellulose-based antioxidant and antimicrobial active packaging film incorporated with curcumin and zinc oxide. *International Journal of Biological Macromolecules* **2020**, 148, 666-676, 10.1016/j.ijbiomac.2020.01.204.
222. Parya Ezati; Jong-Whan Rhim; pH-responsive pectin-based multifunctional films incorporated with curcumin and sulfur nanoparticles. *Carbohydrate Polymers* **2020**, 230, 115638, 10.1016/j.carbpol.2019.115638.
223. Ayca Aydogdu; Clayton J. Radke; Semih Bezci; Emrah Kirtil; Characterization of curcumin incorporated guar gum/orange oil antimicrobial emulsion films. *International Journal of Biological Macromolecules* **2020**, 148, 110-120, 10.1016/j.ijbiomac.2019.12.255.
224. Chongshan Dai; Yang Wang; Gaurav Sharma; Jianzhong Shen; Tony Velkov; Xilong Xiao; Polymyxins–Curcumin Combination Antimicrobial Therapy: Safety Implications and Efficacy for Infection Treatment. *Antioxidants* **2020**, 9, 506, 10.3390/antiox9060506.

225. Mohammed J. Hakeem; Khalid A. Asseri; Luyao Ma; Keng C. Chou; Michael E. Konkel; Xiaonan Lu; A Novel Mathematical Model for Studying Antimicrobial Interactions Against *Campylobacter jejuni*. *Frontiers in Microbiology* **2019**, *10*, 1038, 10.3389/fmicb.2019.01038.
226. Marco Aurélio Paschoal; Cíntia Maria Zanin Moura; Fabiano Jeremias; Juliana Feltrin Souza; Vanderlei S. Bagnato; Juçaira S. M. Giusti; Lourdes Santos-Pinto; Longitudinal effect of curcumin-photodynamic antimicrobial chemotherapy in adolescents during fixed orthodontic treatment: a single-blind randomized clinical trial study. *Lasers in Medical Science* **2014**, *30*, 2059-2065, 10.1007/s10103-014-1700-7.
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