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## Photosensitive nanocomposites: environmental and biological applications

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### ABSTRACT

There has been an extensive investigation in the field of optical applications of nanocomposite materials. To prepare photosensitive nanocomposites, an optically functional phase is embedded in a transparent, processable matrix. This provides the opportunity to utilize the optical properties in other forms including fibers and films, which are more technologically important. Due to expansion of optical materials applications, novel transparent materials and optically functional are required. Recent optical nanocomposites and their applications in different areas especially catalysis and drug delivery have been addressed in this paper.

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### 1. Introduction

Incorporation of semiconductor nanoparticles into ceramic, glass, and polymer matrix materials can provide various interesting optical properties such as nonlinearity, luminescence, fluorescence, and absorption [1, 2]. In these nanocomposites, the matrix material acts as a stabilizer for the particles growth as well as their size, while the small particles improve the optical properties. Laser-active composites are produced

by incorporation of ceramic nanoparticles of solid-state laser materials into polymer-based matrix leading to the formation of films amplified by solid-state laser, which were difficult to prepare traditionally. To retain the optical properties of polymer and glass matrices, optically functional small molecules and polymers can also be incorporated in these matrix materials. Potential applications of composites with nanostructures have led to development of transparent materials with excellent mechanical properties, magnetic properties, and unusually high RI [3].

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## 2. Light-responsive systems

It is reported the UV light results in several disadvantages such as limited tissue penetration depth, and phototoxicity. This has made scientists to focus on providing nanoparticle systems that are light responsive in the visible region (400-700 nm), which leads to reduced phototoxicity. In this regard, the near-infrared light triggered DDSs have become increasingly important for enhancing the tissue penetration depth. Moreover, various studies have been performed about light-based advanced systems for photoacoustic and fluorescent imaging, as well as photothermal and photodynamic therapy [4, 5].

## 3. Light-responsive nanocomposites

In order to control the loading of guest substances, manage their release and enhance mechanical properties, a combination of inorganic substrates and light-sensitive polymers in one system has been favored in recent years [6-9]. Biocompatible and readily modifiable nanoparticles of  $\text{SiO}_2$  with new functionalities are promising for drug delivery applications [10]. Light-responsive nanoparticles of silica with average particle size of 70 nm have been produced by covalent conjugation of amino groups with molecules of photoactive o-nitro benzyl bromide on the particles surface [11]. These groups can be covalently bonded to drugs with hydroxyl, phosphate or carboxylic groups. The o-nitro benzyl bromide molecules are transformed into o-nitro benzaldehyde after irradiation of the resulting particles at 310 nm. This leads to an irreversible cleavage of the bond between the drug and particle and subsequent release of the drug. The intracellular drug release could be externally controlled as because of the small size of these particles that enables their penetration into cells. Schematic of an optical nanocomposite [12] is illustrated in Fig. 1.

NIR light exposure results in photothermal effect and an increase in temperature in NIR-responsive systems leading to drug release [13-15]. The temperature increase can simultaneously cause cell death called “photothermal treatment” [16, 17]. Other involved mechanisms are up-converting nanoparticles (UCNPs) and two-photon conversion [18]. These mechanisms are illustrated in Fig. 2 [19].

## 4. Application of optical nano-composite

It is expected that light-sensitive nano-composites attain widespread applications in the industrial and medical fields owing to their great potential. The applications of these light-sensitive nano-composites will be discussed in the following section.

### 4.1. Drug delivery

Intelligent drug delivery systems [20, 21] are able to modulate drug release proportionately to the specific stimuli intensity and can operate in closed or open circuit [22]. By automatic adjusting of the rate of drug release or switching the release on and off, self-regulated or closed-loop systems can detect specific variations in biological variables including concentration of some substances, temperature, or pH through activating or modulating the response. In open-loop systems, the response to particular an external stimulus is made by the drug release in a pulsing way. The drug release in these systems is proportional to the intensity and duration of each stimulus. This mode of release is not affected by the biological environment variables resulting in an explicit and precise triggering of the drug release. Upon the development of drug delivery systems responsive to heat, irradiation, magnetic or electrical field, ultrasound or compression, an exponential increase of investigations on

polymeric and lipid-based architectures is observed in the last decade. The performance of photo-responsive nanocomposites in DDSs is depicted in Fig. 3 [23].

In a study, Zhang et al. [24] synthesized copper sulfide@polydopamine-folic acid/doxorubicin nanoparticles to produce a novel nanocomposite platform for chemotherapeutic and photothermal tumor-targeting treatment. Compared to CuS/polydopamine, the nanocomposite platform had higher efficiency of photothermal conversion and ultrahigh loading levels.

In another research by Cie et al. [25], the synergistic use of metal organic frameworks (MOFs) and UCNPs for the production of smart nanocomposites was investigated to be applied for photodynamic therapy against hypoxic tumors with high efficiency, which offers novel ways for MOF materials applications in effective cancer treatment. They believe that their research will provide new opportunities for the production of nanocomposites based on MOFs that integrates both multiple functionalities of encapsulated active parts and the synthetic tunability of MOFs. It is expected that the proposed strategy could reveal the extensive potential of MOFs for addressing challenges in other therapies.

Ghavaminejad et al. [26] proposed that the mussel-inspired nanocomposites they produced had controllable multidrug release and excellent heating properties, which can be offered as promising materials for cancer treatment due to the chemotherapy and photothermal therapy (PTT) synergistic effect. The nanocomposites were composed of a stimuli responsive hydrogel (poly(N-isopropylacrylamide) -co-polyacrylamide) incorporated with dopamine nanoparticles that is an effective photothermal agent. The loading drugs were doxorubicin (DOX) and bortezomib (BTZ).

Wang et al. [27] synthesized a novel photo-responsive nanocomposite composed of indocyanine green (ICG), DOX, and graphene oxide (GO)-polyamidoamine-pluronic F68 (PPF68). The nanocomposite was fabricated by cross-linking of graphene oxide with ICG and DOX and the formation of diselenide bond with PPF68. Contrary to commonly used nanomaterials, which are responsive to stimuli received from surrounding environmental, this synthesized nanocomposite responds to the reactive oxygen species (ROS) production via NIR by itself. The nanocomposites have the capability of selective accumulation in tumor cells. The lysosomal escape can occur due to enhanced ROS level and the high proton sponge effect resulting from polyamidoamine (PAMAM). The production of ROS by ICG can induce the diselenide bond cleavage under NIR laser irradiation, which triggers the decomposition inside tumor cell. As a result, before the drugs flow out by P-glycoprotein (P-gp) of multidrug resistant (MDR) tumor cells, the drug secretion could timely reach the therapeutic level. Finally, DOX nuclear trafficking is achieved to kill the MDR tumor cells in an effective way. Furthermore, the overall tumor therapeutic efficacy could be greatly enhanced with combining photothermal therapy and favorable on-demand chemotherapy. These NIR-responsive nanocomposites are shown to be successful in overcoming the MDR of tumor both in-vivo and in vitro, which provide promising novel strategies for clinical MDR cancer therapy.

Based on Nesić et al. [28] research, the nanocomposite based on nanoparticles of  $\text{TiO}_2$  as carrier and ruthenium complex with potential anticancer behavior have light controllable release characteristics. The prepared nanocomposite demonstrated biological activity and free radicals were generated. The free radicals are known as efficient tumor cell killers. The transition metal complex was released consistently from the surface demonstrating the controlled drug delivery system. Additionally, Ru-complex secretion from the surface of  $\text{TiO}_2$  nanoparticles is believed to be dependent on the applied laser (green light) energy. Hence, these properties introduce these nanocomposite materials as suitable candidates for the photo-responsive chemotherapy. Fig 4 summarizes the results of the Hu et al. research [29]; they developed a novel, low-toxic, multifunctional QD-rGO nanocomposite to perform as a photothermal

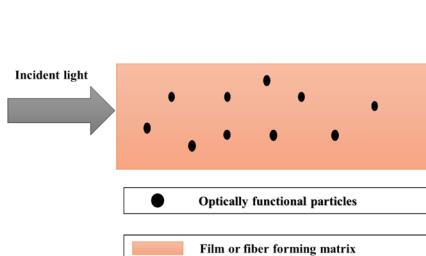


Fig. 1. Schematic of optical nanocomposite.

cancer-therapy agent in the NIR region and an imaging agent in the region of visible-light.

Chen et al. [30] also manufactured effective nanoplatforms of GO and reduced graphene oxide (rGO) nanomaterials for NIR-based PTT. In addition, many reports have demonstrated successful cancer therapy in-vivo and in-vitro with nanomaterials based on graphene as PTT agents, and also their combination with chemical conjugations, surface modification, ultrasound, imaging-guided, PDT, and chemotherapy to improve the therapeutic efficacy and tune their properties in biological systems [31]. In recent years, there have been novel therapeutic methods/strategies and more functionalized nanocomposite based on graphene to improve the therapeutic efficiency of PTT. For modification of the nanocomposite materials based on graphene with highly efficient drug release, imaging-guided therapy, and multifunctional biological characteristics in a single system with the aim of achieving an efficient PTT and promoted cancer synergistic treatment, different inorganic nanoparticles and functional organic macromolecules have been conjugated on the graphene including magnetic iron oxide nanoparticles (IONPs), silica, Au, and DNA.

Nanocomposite hydrogel prepared by Xu et al [32] showed a homogeneous 3D porous structure with steady, slow release rate of DOX during one month. The drug release from the prepared hydrogel had pH-responsive property. This behavior was originated from the acid-labile hydrazone bond cleavage between adamanyl group and DOX, which occurs in acidic environment. The release of loaded drug from the nanocomposite can be accelerated by NIR irradiation. Graphene nanoribbons (GNRs) photothermal effect causes the collapse of the hydrogel networks controlled by the drug release. The excellent photothermal effect and biocompatibility of the prepared hydrogel were confirmed by the in vitro cytotoxicity test. Additionally, the mouse model study revealed that the hydrogel formed in-situ had promising tissue biocompatibility. According to the in vivo antitumor test, nanocomposite hydrogel showed its capacity for synergistic therapy of chemo-photothermal with less adverse effects as a result of efficient photothermal effect and long retention of drug in the tumor site. Thus, this injectable hydrogel, responsive to NIR and pH, could be suggested as a promising material for a long-lasting drug release for chemo-photothermal combined cancer treatment.

Chen et al. [33], developed a mechanically strong and biocompatible nanocomposite hydrogel based on PNIPAM/clay/ carboxymethyl chitosan (CMCTs)/ genipin nanoparticles (GP) using free radical polymerization process with the help of the UV light irradiation, which was responsive to both temperature and pH. To produce the nanocomposites, the natural molecular-genipin and clay were used as the cross-linkers. Under the optimum conditions and high UV light power, the hydrogels demonstrated a high value of tensile strength and the failure strain of about 137.9 kPa and 446.1%, respectively. The synthesized nanocomposite showed high-energy absorption in stretching processes. In the first loop at the room temperature, the nanocomposite was able to recover 76.1% of the adsorbed energy in 15 min after the removal of the load. In addition, the swelling/deswelling properties of the obtained nanocomposites were dependent on the content of GP, CMCTs, and clay. More-

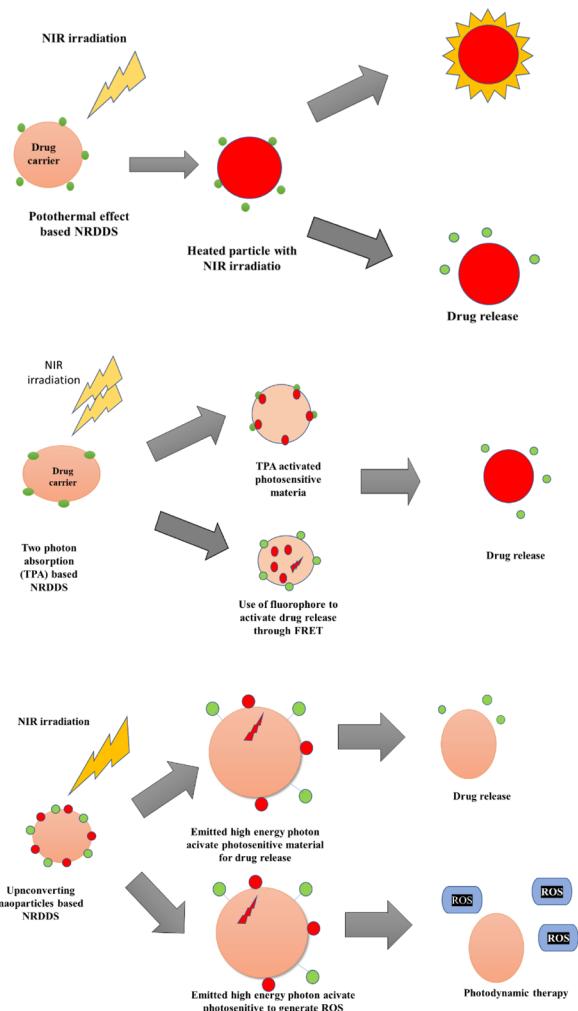
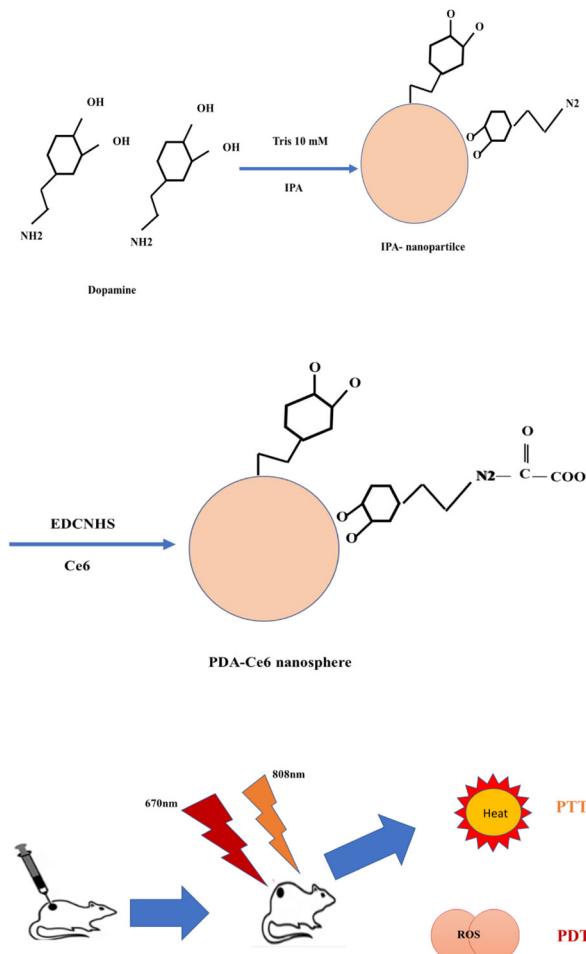


Fig. 2. A scheme of three mechanisms of NIR-responsive drug delivery systems (DDSs).

over, it was shown that the synthesized hydrogels had a controlled aspirin release by regulating the density of crosslinks. According to the results, this promising property suggests these nanocomposites as proper carriers for controlled drug delivery applications.

A new light-responsive nanocomposite based on GO/Polyhedral oligomeric silsesquioxane (POSS) was synthesized by Teng et al. [34]. The synthesis was based on the reversible host-guest inclusion/exclusion method. Supramolecular assembly/disassembly property was observed upon visible and UV irradiation in graphene oxide nanosheets and POSS nanocage. Furthermore, the GO/POSS nanocomposites demonstrated a significant influence on oxygen permeability and good water dispersion in conventional films coated with polyvinyl alcohol (PVA) under different conditions of light irradiation. This could be helpful for development of smart materials as gas barriers in packaging.

To design tumor-targeted photo-controlled drug delivery, Luo et al. [35] developed a nanocomposite based on mesoporous silica/gold (MSN/Au). In the nanocomposites, gold nanoparticle (AuNP) and MSN acted as indicators and carriers, respectively. Photo-switchable azobenzene (Azo) moieties were employed to immobilize the MSN drug carrier. Poly (ethylene glycol) and a matrix metalloproteinase (MMP) substrate were used to modify the fluorescence-quenched gold nanoparticles. An  $\alpha, \beta$  cyclodextrin dimer bridge connected the two types of nanoparticles. According to in vitro investigations, the specific interaction of the prepared nanocomposite with tumor region was observed overexpressing matrix metalloproteinase-2 (MMP-2) enabling the UV light guidance to release the entrapped drug. The integration of MSN-based drug carrier as well as the Au-based indicator could lead to the precise localization of

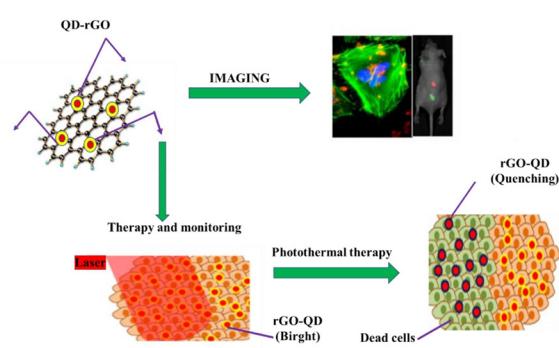


**Fig. 3.** Illustration of photodynamic therapy (PDT), using a combination of light and chemical photosensitizers (PS).

the released drug to tumor region and significant improvement of therapeutic efficacy.

Shi et al. [36] produced NIR-responsive nanocomposite hydrogels based on poly (N-isopropylacrylamide) (PNIPAM)/GO. To prepare the nanocomposites, they combined physically cross-linked graphene oxide nanosheets with chemically cross-linked small molecules. The excellent NIR response of the prepared hydrogels was originated from combining the polymeric networks of thermoresponsive PNIPAM and GO nanosheets. Incorporation of a low concentration of N,N'-methylenebis(acrylamide) (BIS) molecules for the formation of chemical cross-links in the hydrogels led to the formation of a relatively homogeneous structure with rare dense clusters containing chemical cross-links and flexible long polymer chains and, subsequently, the ultrahigh tensibility. Additionally, a further increase in hydrogel toughness could be achieved by hydrogen bond interactions and physical cross-linking generated among the amide groups existing in PNIPAM chains and oxidized groups of GO nanosheets. This synthesized nanocomposite with ultrahigh tensibility demonstrated fast, repeatable, and reversible NIR response that made them remarkably promising candidates for producing artificial muscles, smart actuators, and remote light-controlled devices.

As mentioned, graphene oxide and their nanocomposites are attracting attention in both photothermal therapy and drug delivery due to having high specific surface area as well as high NIR-optical absorption. In this regard, Li et al. [37] integrated (c,c,t-[Pt(NH<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>(OH)<sub>2</sub>]) complex and PEGylated nano-graphene oxide (PEG-NGO) into a single platform (PEG-NGO-Pt) to produce a multifunctional nanocomposite. The nanocomposite showed capability of synergic photothermal-chemotherapy and targeted drug delivery using NIR laser irradiation, and



**Fig. 4.** rGO nanocomposites tagged with quantum dot (left) entered into targeted cancerous cells emit bright fluorescence from the quantum dots, (right); the absorption of NIR radiation by rGO and its conversion into heat, causing fluorescence reduction and cell death (Reproduced with permission [29]).

real-time monitoring with high therapeutic efficacy. The nanocomposite therapeutic influence on cancer therapy was improved by apoptosis and cell death. As a result of the high potential of specific tumor targeting at higher temperatures and the improved cisplatin cytotoxicity, the therapeutic efficacy improvement of the loaded drug accompanied by complete destruction of tumors was proved. Compared to photothermal or chemotherapy treatment alone, minimal systemic toxicity and no tumor recurrence were observed indicating the beneficial influences of GO and Pt (IV) integration for anticancer therapy.

Using the PEG double acrylates (PEGDA) macromers gelation, Xia et al. [38] constructed porous nanocomposite hydrogels based on silicon. Under NIR irradiation, photosensitization of porous silicon nanoparticles (PSiNPs) with singlet oxygen was initiated. Sustained drug release with high efficiency, significant photothermal effect, excellent biodegradability, and strong fluorescence of multifunctional PSiNPs/PEGDA hydrogels were indicated. Eventually, NIR light induced the hydrogels *in situ* growth in tumor cells providing a remarkable localized prevention for the adherence, viability, and tumor cells migration. Hence, they proposed that the fabricated hybrid hydrogels could be potential material for local cancer treatment in clinical practice in the future.

Yang et al. [39] grafted lactose acid (LA) onto polydopamine (PDA)@cobalt phytate (CoPA) to produce a novel multifunctional nanocomposite for photothermal therapy and photothermal imaging of cancers. The role of PDA core was to provide a template for the CoPA formation. The dual photo-responsive abilities of CoPA shell included induction of singlet oxygen formation as well as in-situ production of O<sub>2</sub> through catalyzing intracellular water splitting, which enhanced photodynamic therapy influence on cancer cells under laser irradiation. Moreover, the LA grafting provided the synthesized nanocomposites with the targeting ability to determine particular targeted cancer treatment. The excellent synergistic PDT and PTT effect of PDA@CoPA-LA nanoparticles demonstrated their potential in the clinic cancer therapy applications.

Using facile and scalable solvothermal method, Ma et al. [40] synthesized CdS/rGO nanocomposites for efficient anticancer treatment. According to morphological analysis, CdS/rGO nanoflakes were formed by firm attachment of the spherical CdS nanoparticles on the rGO thin sheets. The cell survival cytocompatibility of the CdS/rGO nanomaterials obtained from the live-dead assay method was indicated to be above 95% revealing their suitability for the cancer treatment. The improvement of CdS/rGO nanoflakes temperature profile under the NIR radiation accelerated the cancer cell death. It was suggested that the proposed nanocomposites with anticancer activity could provide opportunities in biomedicine research to produce efficient materials for clinical applications.

cations.

In another study, Gorgizadeh et al. [41] synthesized MnFe<sub>2</sub>O<sub>4</sub>/C nanocomposite with uniform spherical particles and cracked surface with the average particle size of 221.6 ± 22 nm. Saturation magnetization, coercivity, and magnetic moment of MnFe<sub>2</sub>O<sub>4</sub>/C nanocomposite were 13.250 emu g<sup>-1</sup>, 13.204 G, and 0.55, respectively. Cubic spinel MnFe<sub>2</sub>O<sub>4</sub> dots with the diameter of 2.1 ± 0.6 nm were embedded in carbon entity. The nanocomposite acted as a new absorbing agent of both ultrasound (US) wave and 808 nm laser light in treatment of mice with melanoma tumor and C540 cancer cells. MnFe<sub>2</sub>O<sub>4</sub>/C nanocomposite can also be used in magnetic resonance imaging as a contrast agent. Although MnFe<sub>2</sub>O<sub>4</sub>/C showed relative biocompatibility, their effect on the tumor cells was negligible at US waves of 1.0 MHz and 808 nm laser light. The activation of nanocomposites to kill the C540 cancer cells occurred at US waves along with the laser light at power densities of 1.0 and 0.5 W cm<sup>-2</sup>. At these power densities, cell viability upon irradiation of both US and the laser light in the presence of 25 µg mL<sup>-1</sup> nanocomposite reached 4.6% and 21.5, respectively. Moreover, intra-tumoral injection of the nanocomposite accompanied by US and laser light irradiations indicated via histological analyses resulted in a deep tumor tissue necrosis. Its potential theranostic effect in nanomedicine is apparent owing to its SDT and PTT efficacies as well as a highly contrast induction in MRI.

Liu et al. [42] fabricated rGO-hybridized PEG smart hydrogel and optimized their pH and NIR-responsive drug release properties for cancer therapy. The reason for selecting rGO was to improve photothermal property of the hydrogel [43, 44]. The results of study by Tan et al. [45] demonstrated that the injectable Dox/celecoxib (Cel)/MOFs@Gel nanocomposite showed remarkable biological abilities such as enhanced biocompatibility, antitumor efficacy, and pH-responsiveness suggesting this nanocomposite as an appropriate carrier for local oral cancer therapy.

Using NIR-responsive polymers (HAMAFA-b-DDACMM) coating on the nanoparticles of hollow mesoporous SiO<sub>2</sub>, which was modified by octadecyltrimethoxysilane (C18) (HMS@C18) through self-assembly, Lin et al. [46] fabricated novel multifunctional nanovehicles for cell imaging and tumor treatment. HMS@C18 was selected as the core due

to enhancement of biological stability and the drug loading capacity; the loading efficiency of which was higher than 70%. As a result of the light-responsive copolymers degradation under NIR light excitation at 800 nm, the pre-loaded nanocomposites could release the drug. The correlation of the release efficiency with the light power and irradiation time was also indicated. Based on in vitro investigations, the cancer cells over-expressing FA receptor (FR (+)) like KB cells by endocytosis were easily targeted by the prepared nanocomposites. Additionally, strong fluorescence of the copolymer provided the ability to track the drug delivery process.

Wang et al. [47], integrated stimuli-responsive release property and magnetic targeting by the synthesis of a new smart core-shell drug delivery system using magnetic mesoporous SiO<sub>2</sub>, which was coated by light-responsive azobenzene derivatives with covalent grafting. The loaded molecule release in the mesopores was triggered by visible light irradiation.

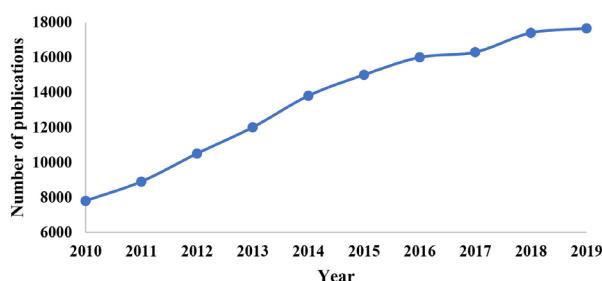
In another research, Jiang et al. [48], synthesized composite nanoparticles of Au/mesoporous SiO<sub>2</sub>/rhodamine B isothiocyanate. These nanoparticles with well-defined mesoporous structure were shown to be suitable for drug loading and they showed strong absorption of infrared surface plasmon for light-controlled drug delivery as well as photothermal cancer treatment; thus, they could be functionalized for fluorescence imaging. This new nanomaterial can open an avenue in chemotherapy of cancer by synergistic use of hyperthermia and cell imaging.

According to Dong et al. [49], core/shell nanoparticles of superparamagnetic Fe<sub>3</sub>O<sub>4</sub>/Au with tunable optical properties and sizes were developed by a facile seed-mediated growth method. For the synthesis of the nanoparticles, gold seed were formed and attached on the surface of the core by Au-S covalent bonding, which were created in a simultaneous reaction in the one-pot operation. This synthesized nanocomposite was proposed to deliver an enhanced capability of localized photothermal tumor treatment and MRI under NIR laser radiation.

In a study by Zhang et al. [50], DOX was loaded into nanospheres composed of UCNPs@mSiO<sub>2</sub>-poly(N-isopropylacrylamide-comethacrylic acid) (NIPAm-co-MAA). The prepared composite drug delivery system showed a significant improved drug release at low pH values and

**Table 1.** Optical nano-composite applied in the field of drug delivery

| Author               | Optical nano-composite  | Application  | Ref. |
|----------------------|---|--|------|
| Wang et al.          | AuNR@SiO <sub>2</sub> /Ce@polydopamine@aptamer nano-composite   | Enhancing treatment of non-small cell lung cancer  | [55] |
| Zhang et al.         | Se@SiO <sub>2</sub> -FA-CuS nanocomposites  | Chemo-Photothermal Cancer Therapy  | [24] |
| Cai et al.           | UCNPs/MB@ zeolitic imidazolate framework (ZIF-8)@catalase smart nanocomposite with core-shell structure | Efficient H <sub>2</sub> O <sub>2</sub> /NIR -responsive PDT agent for hypoxic tumor cells treatment                       | [25] |
| Ghavami Nejad et al. | Nanocomposite Hydrogel  | Chemo-Photothermal Cancer Therapy  | [26] |
| Yu et al.            | Rattle-type gold nanorods@void@porous-SiO <sub>2</sub> (GVPSPR)-DOX/tetradecanol (TD) nanocomposites    | Chemo-Photothermal Cancer Therapy  | [56] |
| Wang et al.          | ICG/DOX/GO-PPF68 NIR-responsive nanocomposite   | Clinical treatment of MDR cancer   | [27] |
| Nešić et al.         | Nanocomposite system made of colloidal TiO <sub>2</sub>   | Potential controlled metallo-drug delivery   | [28] |
| Niu et al.           | Polydimethylsiloxane (PDMS)/GNPs nanocomposites   | drug-delivery, microswitches, and soft robotics  | [57] |
| Chen et al.          | Graphene-derived nanocomposites   | Photothermal therapy of tumor treatment  | [30] |
| Xu et al.            | (NIPAm-co- methacrylated poly-β-cyclodextrin (MPCD))/GNRs nano-composite                                | Chemophotothermal synergistic cancer therapy   | [32] |
| Chen et al.          | Nanocomposite double network PNIPAM/clay/CMCTs/GP   | Controlled drug release of aspirin   | [33] |
| Teng et al.          | GO-POSS nanocomposites  | Host-guest inclusion / Oxygen permeability   | [58] |
| Luo et al.           | Mesoporous silica/gold (MSN/Au) nanocomposite   | Controlled drug delivery system  | [35] |
| Shi et al.           | PNIPAM-GO nanocomposite   | Artificial muscles, smart actuators, and remote light-controlled devices   | [36] |
| Li et al.            | Pt(IV) complexes/PEGylated GO sheets multifunctional nanocomposite                                      | A synergistic effect in the therapeutic efficacy improvement of Pt drug using combined chemotherapy photothermal treatment | [37] |



**Fig. 5.** Research reports focusing on optical nano-composite for purification of wastewater based on scholar-google database.

high temperature, which exhibited an apparent pH/thermo controlled drug release. These hybrid nanospheres could also be employed as bio-monitors and bioimaging agents for tracking the drug release extent. Simultaneous stimuli-responsive drug delivery and imaging suggest these materials as a novel and reliable multifunctional nanocarriers.

Zhu et al. [51], synthesized a photo-responsive nanocomposite hydrogel based on PNIPAM/GO by in situ polymerization using  $\gamma$ -irradiation. Different levels of GO doping in the hydrogel led to a change in colors and phase-transition temperatures. The prepared hydrogel showed great photothermal properties as a result of the high value of optical absorbance of the GO. It was possible to control phase transitions by irradiation of NIR laser. The rate of NIR-induced temperature increased with GO loading amount and the temperature could be adjusted effectively by the duration of irradiation. It was proposed that the prepared nanocomposite with its excellent photothermal properties could be used in the biomedical applications, particularly as microfluidic devices and the easy synthetic method could be employed to synthesize other nanocomposites.

A novel Au nanorod (AuNRs)/NGO core/shell nanostructure was developed by Xu et al. [52] as an efficient agent for chemophotothermal cancer therapy. The role of NGO shells was to reduce the toxicity of AuNRs coated with surfactant and create anchor sites for conjugating the hyaluronic acid. Higher photothermal efficiency and the potential of targeting hepatoma Huh-7 cancer cells was achieved for the HA-conjugated nanocomposites (NGOHA-AuNRs) compared with AuNRs. DOX-loaded NGOHA-AuNR exhibited pH-responsive and triggered the drug-release with near-infrared light irradiation. In comparison with single photothermal therapy and chemotherapy, combined chemo-photothermal therapy showed higher rates of cancer cell death, with biosafety to nontargeting cells.

The PEG-GO/CuS nanocomposites synthesized by Bai et al. [53] showed excellent biocompatibility with high photothermal conversion efficiency, high anticancer DOX storage capacity, and capability of the tumor ablation. The DOX-loaded nanocomposites demonstrated higher toxicity compared to pure nanocomposites and free DOX under NIR laser irradiation, due to both cytotoxicity of DOX release triggered by light and photothermal ablation mediated by PEG-GO/CuS. According to mouse models investigation, the chemo-photothermal influence of DOX-loaded nanocomposites led to significant inhibition of mouse cervical tumor growth and an effective tumor cell reduction. In general, the synergistic therapy demonstrated higher therapeutic efficacy in comparison with photothermal and chemotherapy treatment alone.

A DNA cross-linked polymer was coated on Au–Ag nanorods by Kang et al. [54] for a NRI-responsive drug delivery system. In order for gel scaffold to encapsulate anticancer drugs, DNA has been cross-linked for development of a sol–gel transition system based on polyacrylamide. By functionalization with targeting moieties like aptamers, nanohydrogel could specifically recognize tumor cells. The photothermal effect induced by NIR irradiation made the temperature of the surrounding gel increase rapidly, which led to the quick and controlled drug release with

spatial/temporal resolution.

#### 4.2 Purification of water pollutants

Due to increasing pace of industrialization, there are serious concerns about water pollution that creates major damages to human beings and microorganisms [59–61]. Several industries produce textile and other industrial dyes that can contaminate the fresh water. Moreover, due to containing highly toxic organic substances, these industrial dyes are considered as major water pollutants [62, 63]. Thus, researchers around the world consider the removal of industrial organic contaminants as the most urgent action. One of the green approaches for complete elimination of organic contaminants is semiconductor photocatalysis. In these photocatalysts, solar energy sources can be used without creating any secondary pollution [64–66]. Metal oxides especially ZnO and TiO<sub>2</sub> are commonly utilized photocatalysts for purification of wastewater owing to their strong photo-stability, non-toxicity, low-cost, and more availability [67]. Fig. 5 depicts the volume of research conducted in water purification field over the past decade.

Shi et al. [68], produced novel carbon nanotubes (CNTs) photocatalysts loaded with Ag/AgX (X = I, Br, and Cl) composite using a facile deposition–precipitation route with ultrasound. According to the results, the direct interfacial contact between CNTs and Ag/AgX nanoparticles was observed exhibiting superior visible light absorbance because of the Ag surface plasmon resonance (SPR). These produced composite photocatalysts were able to eliminate 2, 4, 6-tribromophenol (TBP) in aqueous phase. In comparison with pure CNTs or AgX, the nanocomposites showed a significant improvement in visible light photocatalytic degradation efficiency because they effectively transfer electron from plasmon-excited Ag (0) and photoexcited AgX nanoparticles to CNTs. As a result, a prolonged photoholes lifetime and enhancement of the degradation efficiency could be achieved due to effective reduction of electron–hole recombination.

Using a hydrothermal process, Yue et al. [69] produced a visible-light-sensitive heterojunction photocatalyst with the formula of Bi<sub>2</sub>MoO<sub>6</sub>–BiOCl. The as-prepared composite showed an irregular multi-plate structure composed of BiOCl and Bi<sub>2</sub>MoO<sub>6</sub> nanoplates over each other. Compared to pure Bi<sub>2</sub>MoO<sub>6</sub> and BiOCl, the synthesized photocatalyst showed higher photocatalytic activity. 30% Bi<sub>2</sub>MoO<sub>6</sub> content was found to be optimal for the photocatalytic activity of the composites. The O<sub>2</sub> and OH<sup>–</sup> had the main roles in rhodamine B (RhB) degradation through the Bi<sub>2</sub>MoO<sub>6</sub>–BiOCl composite.

In another study, Hamid et al. [70] synthesized a UV-visible light-responsive nanophotocatalyst composed of TiO<sub>2</sub> and multiwalled carbon nanotube (MWCNT). The nanocomposites were produced via a modified sol–gel technique by functionalized MWCNTs and titanium isopropoxide as the initiating precursors. It was indicated that the surface of the MWCNTs were coated by TiO<sub>2</sub> nanoparticles with a diameter of 10–20 nm. MWCNT/TiO<sub>2</sub> and pure TiO<sub>2</sub> nanoparticles had the specific surface areas of 181 and 80 m<sup>2</sup>/g, respectively. Therefore, photocatalytic performance of MWCNT/TiO<sub>2</sub> was better compared to pure TiO<sub>2</sub> due to higher surface area leading to functioning as enhanced electron acceptors and electron–hole pair recombination inhibitors. Other reports have also highlighted the CNT/TiO<sub>2</sub> nanocomposites [71].

Photocatalytic performance under visible light radiation for the degradation of RhB by g-C<sub>3</sub>N<sub>4</sub>–Fe<sub>3</sub>O<sub>4</sub> nanocomposites synthesized by Kumar et al. [72], exhibited remarkable improvement. Based on the obtained results, the nanocatalysts could be magnetically recovered and exhibited good recyclability while keeping their photocatalytic activity after six cycles. The high photocatalysts activity of the nanocomposite is because of improved charge-separation properties, high visible-light-absorption efficiency, and the large surface-exposure area. Additionally, the nanocomposites possessed superparamagnetic properties suggesting

them as promising candidates for bionanotechnology and lithium storage capacity applications.

Research investigation on Cu-doped ZnO/carbon nanotube nanocomposites by Ahmad et al. [73] showed effective MO bleaching out which was the indicator of a significant photocatalytic improvement over ZnO, ZnO/CNTs, and Cu-doped ZnO nanoparticles. Based on the results, the organic molecules were completely destroyed with color disappearance and the significant reduction in chemical oxygen demand of the treated effluent. The large surface area and excellent electrical properties of CNTs caused increased charge/separation efficiency, extended light absorbing capability, and higher dyes adsorptivity and, eventually, dramatic improvement of nanocomposite photoactivity.

Another visible-light-induced photocatalyst fabricated by a simple solution method is Ag<sub>2</sub>O/GO nanocomposite. During Ag<sub>2</sub>O/GO nanocomposite formation, negatively charged GO sheets interact electrostatically with positively charged Ag<sup>+</sup>. The synthesized nanocomposites demonstrated promoted photocatalytic activity compared to Ag<sub>2</sub>O nanoparticles because of the enhanced electron–hole pair separation, smaller sizes of the Ag<sub>2</sub>O nanoparticles, and the enhanced adsorption capacity. The obtained results open new avenues to design photocatalysts with high efficiency for eliminating organic contaminants from water [73].

Tongon et al. [74] incorporated Ag-doped TiO<sub>2</sub> into mesostructured silica (MCM-41) by a microwave assisted sol–gel route for the preparation of a nanocomposite film with visible light responsive property. High photocatalytic properties and adsorbability of the TiO<sub>2</sub> photocatalyst improved by MCM-41 and Ag were observed. Ag/Ti/Si with the composition of 0.1/1/2 showed methylene blue (MB) decolorization efficiency equal to 30% under visible light, and 81% under UV light.

Ong et al. [74] prepared solvent exfoliated graphene (SEG)/ZnO photocatalysts using a simple chemical deposition-calcination method. The Reactive Black 5 (RB5) degradation of prepared nanocomposites were 97% and their rate constant was 0.0199 min<sup>-1</sup> under an energy-saving light bulb which was indicated to be more than that of ZnO and SEG. The ZnO content of 69.0 wt. % in the nanocomposite showed a significant improvement after graphene hybridization compared to pure ZnO. The enhancement was reported to be due to electron–hole recombination retardation and effective dye sensitization by SEG as electron storage.

The CdS/La<sub>2</sub>Ti<sub>2</sub>O<sub>7</sub> photocatalyst nanocomposite was produced using a sonochemical coupled technique. This nanocomposite demonstrated a strong photocatalytic decomposition of methyl orange (MO) under visible light and UV radiation. The highest photocatalytic activity was obtained for the sample with La to Cd ratio of 1:3. The improved photocatalytic property of this nanocomposite was proposed to be related to the matched band potential of the two semiconductors and the layered structure of the nanocomposite [75].

Zhu et al. [76] used GO nanosheets to enwrap Ag/AgX (X = Cl, Br) nanocomposites using a water/oil system. The prepared hybrid nanocomposites had the potential to be employed as a stable plasmonic photocatalyst for degradation of MO by visible-light radiation. Ag/AgX/GO nanocomposites displayed improved photocatalytic activities in comparison with the Ag/AgX nanocomposites. Incorporation of GO nanosheets caused the retarded electron–hole pairs recombination, the facilitated charge transfer, the smaller Ag/AgX nanoparticles, and the nice adsorptive capacity to MO molecules leading to promotion of photocatalytic performance of Ag/AgX/GO. Based on these obtained results, developing graphene oxide-based plasmonic photocatalysts with high efficiency and stability would be possible.

In another research, nanocomposites of SnS<sub>x</sub>/SnO<sub>2</sub> consisting of different SnO<sub>2</sub> contents were produced by in situ hydrothermal oxidation of tin sulfide nanoparticles. According to the results, the synthesized nanocomposites with optimum amount of SnO<sub>2</sub> showed remarkable photocatalytic stability as well as higher photocatalytic activity in

comparison with SnS<sub>x</sub> nanoparticles and the physical mixture of SnO<sub>2</sub> and SnS<sub>x</sub> nanoparticles. The high photocatalytic performances of SnS<sub>x</sub>/SnO<sub>2</sub> nanocomposites relates to bonding of SnO<sub>2</sub> to SnS<sub>x</sub> particles through which electron transfer at the interface could be facilitated and the self-agglomeration of the particles could be reduced [77].

Dong et al. [78] used an in situ photoactivated method to fabricate AgBr/Ag nanocomposites in which Ag nanoparticles deposited evenly on the AgBr surface. Exposing to the irradiation of direct sunlight or cool daylight fluorescent lamp, the prepared nanocomposites revealed superior visible light photocatalytic performance against organic pollutant decomposition even under the diffuse indoor daylight. Moreover, the nanocomposites showed higher stability.

TiO<sub>2</sub>(TiO<sub>2</sub>–V<sub>2</sub>O<sub>5</sub>)/polypyrrole (PPy) nanocomposites were synthesized by Piewnuan et al. [79] using in situ polymerization. According to the results, the absorbance of the nanocomposites was higher than those of neat TiO<sub>2</sub> and TiO<sub>2</sub>/PPy due to the reduction in the band gap energy of the materials. The nanocomposite catalytic activity was also continued in the dark. The mentioned behaviors are caused by capability of the polymer to act as a binder in the system and the energy storage ability of V<sub>2</sub>O<sub>5</sub>.

Gu et al. [80] incorporated reduced graphene oxide in N-doped TiO<sub>2</sub> (N–TiO<sub>2</sub>) as well as V co-doped TiO<sub>2</sub> (N, V–TiO<sub>2</sub>) using a hydrothermal method. Both nanocomposite exhibited superior visible light photocatalytic performance compared to N, V–TiO<sub>2</sub> and N–TiO<sub>2</sub>. The reasons for such enhancement included minimizing the photoinduced electrons and holes recombination, high light absorption intensity, more excited states, and improvement of pollutants adsorption under visible light irradiation.

Pakula et al. [81] synthesized metal/ poly(methylmethacrylate) (PMMA) nanocomposites with light-controlled conductance switching property. The nanocomposites preparation was carried out by physical vapor deposition of Pt and Au clusters on azo-dye doped poly(methylmethacrylate) thin film. Functionalizing the azo groups with branches and tails caused high dye concentrations, which enhanced solubility. Under alternating irradiation of blue light and UV, a complete reversible optical switching of the absorption bands of the nanocomposites was observed.

Graphene quantum dots (GQDs) [82], functionalized by polyethylenimine (GQD-PEIs) nanocomposites were produced by Liu et al. [83] using hydrothermal method. Subsequently, by the amidation reaction of the PEI moieties with isobutyric anhydride, isobutyric amide (IBAm) groups were anchored on the functionalized GQD. The prepared nanocomposites was responsive to temperature, pH, loaded organic guests, and inorganic salts. The modulation of cloud point temperature (T<sub>cp</sub>) of the composites in aqueous solutions was reported to be done by altering the inorganic salts type, pH, the inorganic salts concentration, loaded organic guests, and the number of IBAm units in the nanocomposites. It was indicated that the nanocomposites were photoluminescent, and outside stimuli did not influence their maximum emission wavelengths. A negligibly influence of polar aspirin guest, pH, and traditional salting-out anions such as SO<sub>4</sub><sup>2-</sup> and Cl<sup>-</sup> on emission intensities were observed. It was also verified that the aspirin guest with relative polarity was absorbed by PEI-IBAm shell, while, the PBA guest with relative hydrophobicity was adsorbed by the GOD core. The guest release rate varied below and above T<sub>cp</sub>.

Ren et al. [84] developed a graphene (GR)-CdS nanocomposite using a hydrothermal route in which the GR scaffold closely enwrapped CdS ingredients. They reported that incorporation of two-dimensional GR scaffolds to CdS microspheres had significant influence on hybrid nanocomposites properties including morphology, electronic and optical nature of the nanocomposite. The selective organic transformation results showed that the synthesized nanocomposite could be used as a visible-light-activated photocatalyst for efficient benzyl alcohol oxidation to

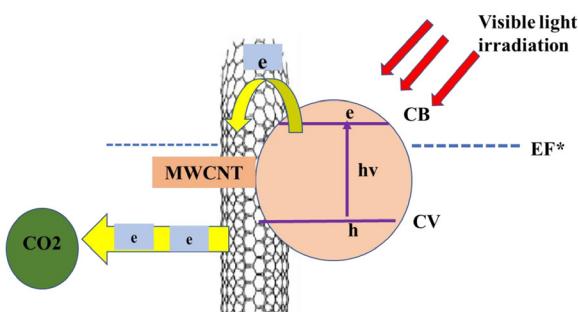


Fig. 6. MWCNT/TiO<sub>2</sub> core–shell nanocomposites.

benzaldehyde at ambient temperature. The combined influence of high electron conductivity and improved light absorption intensity of GR incorporated to remarkably improve the photocatalytic activity of the nanocomposites. These factors increased the lifetime of electron–hole pairs generated by light irradiation and facilitated charge separation. The research could provide the information for production of narrow bandgap semiconductor or GR hybrid nanocomposites applicable for a wide range of photocatalysis.

In a study conducted by Fernández et al. [85], Au nanorods (NRs) were coated by thermoresponsive poly(N-isopropylacrylamide) microgel shells. The investigations by optical extinction measurements and simultaneous laser-heating revealed that the Au cores could be simultaneously utilized for sensitive optical reporting of the microgel state and fast optothermal manipulating (switching) with the possibility of external control in a reversible manner.

Kong et al. [86] functionalized TiO<sub>2</sub> nanoparticles with antifouling ethylene glycol dimethacrylate and biocidal 2-(tert-butylamino)ethyl methacrylate containing nontoxic secondary amine. Compared to pure TiO<sub>2</sub> nanoparticles, core/shell nanoparticles showed higher photocatalytic antibacterial characteristics due to the synergistic antibacterial activity of light-driven biocidal polymer shell as well as TiO<sub>2</sub> core. The prepared nanocomposites showed high antimicrobial efficiency of 95.7% for gram-positive *S. aureus* in the dark condition. Moreover, in comparison with pristine TiO<sub>2</sub> nanoparticles, the nanocomposite demonstrated enhanced inhibition of bacterial growth during UV irradiation.

Woo et al. [87] reported the improved photoluminescence of layered nanocomposites consisting of Sr<sub>2</sub>SiO<sub>4</sub>:Eu green phosphor core, multishell of CdSe/CdS/CdZnS/ZnS red quantum dots, and thermo-curable resin. Two kinds of mixed and layered composite were produced, and the layered structure was found to be more effective compared to the mixed structure in terms of thermal loss, PL decay, and PL intensity. Moreover, by using the layered nanocomposite for preparing white light emitting diodes, the value of color rendering index increased to 88.4 and brightness enhanced by 37% in comparison with the mixed one.

Choi et al. [88], fabricated a dual-responsive nanocomposite including two noble metal nanoparticles and two polymer brushes and reported that they exhibited a significant improvement in selectivity for determining various liquids in comparison with a single-responsive LSPR sensor. Two hydrophilic and hydrophobic polymer brushes provided the dual-responsive LSPR sensor, which showed different response according to the interaction degree among the surrounding liquids and the polymer brushes. Additionally, the accurate estimation of the mixing ratio of two solvents, suggesting the dual-nanocomposite LSPR sensor as in situ process monitoring platform.

Chaengchawi et al. [89] synthesized a visible-light responsive nanocomposite of CdS/ZnO as a photocatalyst. The obtained results demonstrated that the ZnO to CdS ratio had a significant effect on photocatalytic activity among which the highest photocatalytic performance was related to the mole ratio of 1:4 exhibiting higher activity compared to pure ZnO and CdS. A novel ZnO-TiO<sub>2</sub> nanocomposite was also proposed by Haghighatzadeh et al. [90].

Nanocomposites with the composition of TiO<sub>2-x</sub>N<sub>y</sub>/Ag–PbMoO<sub>4</sub> were produced using sonochemical technique. In comparison with Ag–PbMoO<sub>4</sub> and TiO<sub>2-x</sub>N<sub>y</sub>, photoactivation of green tide (*Tetraselmis suecica*) of the synthesized nanocomposites was improved under simulated solar light. The nanocomposites were able to remove 100% of *Tetraselmis suecica* after 25 minutes. By inhibition of electron–hole recombination, the charge transfer was facilitated leading to enhancement of the nanocomposite photocatalytic activity [91].

In a study carried out by Pirhashemi et al. [92], the ZnO/Ag/Ag<sub>2</sub>WO<sub>4</sub> nanocomposites exhibited good photocatalytic activity for RhB degradation. This enhancement was due to the heterojunctions formation among the counterparts and the surface plasmon resonance effect of Ag, which resulted in effective suppression of photogenerated charge carriers' recombination.

A novel nanocomposite for photocatalytic degradation of organic pollutants composed of Ag/CeO<sub>2</sub> was produced by Saravanakumar et al. [93] using hydrothermal method. The nanocomposite showed superior activity with the ability to degrade the RhB dye in 70 minutes, under visible light irradiation. Due to producing a large amount of OH radicals, the photocatalytic degradation enhanced. As a result of the lower charge carriers' recombination, the nanocomposite efficacy was much higher compared to pure CeO<sub>2</sub>. The surface plasmon resonance effect of Ag nanoparticles is a reason for the high photocatalytic activity of nanocomposites.

According to Ahmad et al. [94] study, the incorporation of GO in CdO/GO nanocomposites improved the organic dyes photocatalytic degradation due to provision of more active sites available in high surface area. Highest MB degradation of 95% was achieved for the composition of 3.3% GO after 35 minutes irradiation in comparison with CdO and other compositions. GO inhibits the electron–hole pair recombination, extends the light absorption range, and increase the adsorbability of the catalysts, which leads to photocatalytic efficiency improvement of CdO/GO nanocomposite. It was proposed that these nanomaterials have the potential to be employed for organic pollutants degradations from wastewater.

Hybrid nanocomposite photocatalysts of CuO(x)/SmFeO<sub>3</sub> were prepared by Behzadifa et al. [95]. Because of larger separation efficiency of photoinduced electron–hole pair, the CuO(10 wt%)/SmFeO<sub>3</sub> electrode showed the photocurrent of approximately 2 times more than that of the CuO and SmFeO<sub>3</sub>. The highest photocatalytic efficiency of 65% and the photocatalytic activity of 100% were achieved under visible light radiation for RhB dye degradation exhibiting the existence of both photocatalytic mechanisms and Fenton-like oxidation. Due to being highly active and stable, they suggested the prepared hybrid photocatalyst as a potential material for industrial water treatment.

According to a study by Gan et al. [96], CoFe<sub>2</sub>O<sub>4</sub> incorporated Ag<sub>3</sub>PO<sub>4</sub> nanocomposites with core–shell structure were synthesized using a precipitation method. According to the results, the CoFe<sub>2</sub>O<sub>4</sub> nanoparticles incorporation narrowed the Ag<sub>3</sub>PO<sub>4</sub> band gap. The core–shelled structured nanocomposites showed superior efficiency of dyes degradation under the tungsten halogen lamp light in comparison with pristine Ag<sub>3</sub>PO<sub>4</sub>. Additionally, the nanocomposites exhibited good recycling stability for the dyes photocatalysis degradation and were magnetically separable. Overall, this research offers a new nanocomposite with the capability of photocatalytic degradation of organic contaminants present in wastewater, while does not introduce secondary pollutant into the system.

Using ultrasonic-irradiation technique, Mousavi et al. [97] fabricated g-C<sub>3</sub>N<sub>4</sub>/Fe<sub>3</sub>O<sub>4</sub>/Ag<sub>3</sub>PO<sub>4</sub>/AgCl nanocomposites which had promising photocatalytic activity under visible-light irradiation. This nanocomposite demonstrated higher photocatalytic performance in degradation of RhB than that of g-C<sub>3</sub>N<sub>4</sub>. Because of significant saturation magnetization of 8.78 emu.g<sup>-1</sup>, it was possible to easily separate the photocatalyst from

the solution after treatment by an external magnetic field. It was found that driving the degradation reaction is caused mostly by holes as main active species.

The NiFe<sub>2</sub>O<sub>4</sub>/MWCNTs/ZnO nanocomposite was also fabricated with solar radiation driven photocatalytic activity. Upon solar radiation, the prepared nanocomposite showed a significant enhancement in photocatalytic activity in comparison with ZnO and NiFe<sub>2</sub>O<sub>4</sub> for degradation of MB dye in aqueous solutions. Recombination retardation of electron–hole pairs caused higher charge separation efficiency leading to improved photocatalytic activity. They reported that the apparent rate constant (k<sub>app</sub>) of the MB degradation in 300 minutes using ZnO, NiFe<sub>2</sub>O<sub>4</sub>, and NiFe<sub>2</sub>O<sub>4</sub>/MWCNTs/ZnO were 0.002, 4.12857E-4, and 0.00438 min<sup>-1</sup>, respectively. The magnetic properties of the nanocomposite provide the possibility of its separation and re-usability after degradation experiments. It was suggested that the prepared nanocomposite can be utilized as a solar radiation driven photocatalyst [98].

Paul et al. [99] reported the preparation of a MnMoO<sub>4</sub>/NiFe<sub>2</sub>O<sub>4</sub> nanocomposite using co- hydrothermal and precipitation routes. The synthesized photocatalyst exhibited 95% Basic Fuchsin removal efficiency and superior photocatalytic activity with 96% efficiency for different dyes including Methyl Violet (MV), RhB, and MB degradation in aqueous medium under visible light radiation. Increased agglomerated forms of the synthesized MnMoO<sub>4</sub>/NiFe<sub>2</sub>O<sub>4</sub> nanocomposites were observed in the spent photocatalyst.

Nickel tungstate/tin phthalocyanine (NiWO<sub>4</sub>/SnPc) nanocomposite produced by the solvent evaporation technique showed the enhancement of NiWO<sub>4</sub> photocatalytic property for Rhodamine blue degradation [100].

Core–shell nanocomposites consisted of MWCNT/TiO<sub>2</sub> demonstrated that their photoactivity in the visible light was remarkably improved with extension of absorption edge to the region related to visible light. These nanocomposites showed continuous transformation of CO<sub>2</sub> into methane at atmospheric pressure and under the irradiation of low power visible light. After 6 hours of irradiation, the maximum methane production of ca. 0.17 μmol/g-catalyst/h was achieved. Fig 6 depicts the model used in this article [101].

## 5. Conclusions and future insights

Using light-sensitivity as an attractive property for preparation of advanced DDS that can modulate the rate and site externally. In order to optimize the therapeutic efficiency and reproducible release profiles of the light responsive materials various approaches is currently investigated. In order to use the light-sensitive DDS for clinical practices, considerable additional efforts are required regarding specific aspects including: (1) In vivo analysis of newly developed delivery systems. In order to make progress toward clinical applications, supplementary in vivo studies must be carried out in addition to in vitro investigations. (2) Specialized equipment to provide sufficient irradiation intensity for targeting specific region while does not alter surrounding tissues. Because the human body is to relatively impermeable to the light, applicability of the visible light/ UV-sensitive DDS is limited to treatments of the skin surface layers. Feasible alternatives to light/UV-sensitive DDS appear to be NIR-sensitive light materials and NIR lasers. (3) Design and fabrication of new biocompatible materials for extending the range of light-sensitive polymers and lipids which meet the needs for developing safe products. For example, azobenzene groups are considered as toxic materials by the FDA which constrains the application of such DDS [102].

It is expected that novel nanocomposites with various chemical designs will offer an attractive and insightful approaches to overcome the problems of both ingestion and identification, enhance intertumoral

accumulation and decrease the drugs toxicity to produce high-sensitive materials with high efficiency.

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## Conflict of Interest

All authors declare no conflicts of interest in this paper.

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