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Palladium Nanoarchitectures: Chemistry and Bio-Medicinal Purposes

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Abstract

Metal nanoarchitectures were offered valuable possibilities for targeting drug delivery, diagnosis/detection and bioimaging. However, gold, silver and platinum nanostructures were superiorly applicable in this field, whereas, several hurdles were impeded the wide-scaled applicability of those nano-pharmaceuticals in clinical contexts. Meanwhile, innovative techniques for investigation of alternative metals were recently reported for their potency in medical purposes. Palladium nanoarchitectures are advantageous with superior catalytic and optical activities. But, till now, very few researching reports were taken the advantage of these unique properties for its applicability in the biomedical purpose. The current review is considered with demonstration of the recent reports that considered with studying the applicability of palladium nanoarchitectures in different biomedical purposes. Recently, palladium nanoarchitectures were investigated as photothermal agents, photoacoustic imaging, prodrug activator, biosensing, as and for anti-cancer/anti-microbial therapy. Only with a handful of available researching approaches, the pharmaceutical applicability of palladium nanoarchitectures that are currently reviewed, are in their infancy. Till now their excellent potentiality and toxicity profiles might qualify such nanostructures as future key parameters in the biomedical purposes.

Keywords: Pd nanoarchitectures*; Photothermal; Photoacoustic imaging; Biosensing; Anti-cancer; Anti-microbial.*

1. Introduction

Metal nanoarchitectures are extensively considered in various biomedical purposes attributing to their size and geometry; mechanic, electronic and optical characters; and their outstanding anti-corrosive and anti-oxidative properties [1-3]. Metal nanoarchitectures represent invaluable possibility for unique cancer therapy, drug delivery targeting, diagnosis/detection, and bioimaging [1, 4]. Recently, silver, gold, and platinum nanoarchitectures are widely reported in the biomedical purposes; different approaches were considered the probability for the clinical practicing [5-7]. Additionally, palladium nanostructures were expressed to exhibit excellent physicochemical characters, like the good thermal stabilities, chemical stabilities, photocatalytic activities, electronic activities, optical characters, and cost effectiveness [8-13].

Nanopalladium could be synthesized with various sizes and geometries [8, 14, 15]. They could be capped with other molecules or biopolymers to prepare biocompatible nanostructures with the desirable characters [16-18]. Previous studies have investigated the wide-scaled applicability of nanopalladium in hydrogen storage/sensing [19], organic coupling synthesis [20, 21], fuel cells [22], and sensors [23] (Figure 1). Moreover, nanopalladium are commonly exploited in various purposes depending on its high catalytic performance, like, a catalyst for formation of C-C bond and oxidative processes in the field of pharmaceuticals [24, 25] (Figure 1). On the

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other hand, few studies have demonstrated the applicability of nanopalladium in the biomedical purposes. In recent years, nanopalladium were investigated as antimicrobial agents [26, 27], photoacoustic agents [16, 28, 29], prodrug activators [30, 31], anticancer agents [32, 33], gene/drug carriers [34, 35] and photothermal agents [16, 18, 36, 37].

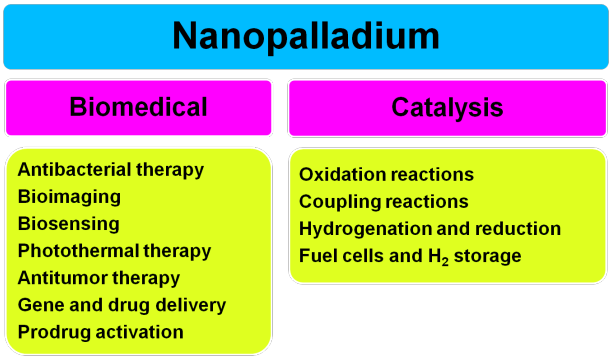

Figure 1: Scheme for applications of palladium nanoarchitectures.

According to our knowledge, there were no review articles about the applicability of palladium nanoarchitectures in the biomedical purposes. Palladium nanoarchitectures were extensively attracted the attention for their exploitation in the field of photothermal therapy attributing to their high thermal stability and optical characters [16, 18, 36, 37]. Photothermal therapy is a new type of therapy through which near-infrared laser photo-absorbers are applicable for generating heat under near infra-red laser irradiation. Whereas, strong absorption in infra-red region of palladium nanoarchitectures greatly enhances the light penetration into the tissue [38]. Exploitation of the optical property for a certain material, photoacoustic imaging is also recently investigated as unique bioimaging methodology for early management and diagnosis of carcinogenic tumor [39, 40]. For enhancement the photoacoustic signals from the tested tissue, the photoacoustic agent is usually required. Palladium nanoarchitectures are recently investigated as photoacoustic agents and the data showed the promising potency of palladium nanoarchitectures as an effective photoacoustic agents for photoacoustic imaging [16, 28, 29]. Another enhanced performance of palladium nanoarchitectures in biomedical purposes is drug/ gene delivery [34, 35].

High surface area for uploading of high amount from the required drug, stability, and nontoxic effects of palladium nanoarchitectures results in their exploitation as efficient nanocarriers for drugs or genes or any other small molecules [34, 35]. With their superior photocatalytic potency, palladium nanoarchitectures were explored as prodrug activators [30, 31]. This mentioned performance was investigated for gemcitabine and 5-fluorouraci (5FU). The mechanism of antitumor performance for palladium nanoarchitectures was recently elucidated and the anticancer action of palladium nanoarchitectures was initially examined against number of cancer cell lines. The effectiveness of palladium nanoarchitectures as superior microbicidal laborers was examined against different bacterial strains [26, 27].

This review acts in motivation for sharing up-to-date works on the potentiality of palladium nanoarchitectures in the biomedical purposes. The most recent reports on the applicability of palladium nanoarchitectures for photoacoustic imaging, infection/cancer PTT, bactericidal applicability, antitumor therapy, drug and gene delivery, biosensor, prodrug activator and multifunctional nanostructures are extensively reported. The overview of toxic effects, pharmacokinetic, and bio distribution of palladium nanoarchitectures was demonstrated. Eventually, a perceptual sign is represented for the future of exploitation of palladium nanoarchitectures in biomedical purposes.

2. Synthesis of palladium nanoarchitectures

Palladium nanoarchitectures can be successfully clustered via chemical, physical, or biogenic methods of synthesis. However, chemical and biogenic routes of synthesis are the common synthetic techniques for production of palladium nanoarchitectures for application in biomedical purposes. The geometry, size, dimensional structure, and stabilization of palladium nanoarchitectures strongly affect on their characterizations and

applications. The emergence of palladium nanoarchitectures for application in biomedical purposes requires their biocompatibility and stable dispersibility in different biological environments. Therefore, researchers interested in this field of study were extensively considered with investigation of simple, environment friendly, energy and cost saving synthetic techniques. The chemical method of synthesis is preferable as the conditions of reaction, including concentration of reactants, additives, pH and temperature could be adjusted, in order to obtain the required nanoarchitecture [41]. It was reported that, both of porous and cube-like palladium nanoarchitectures were ingrained from H_2PdCl_4 as a precursor, $NaBH_4$ as a reducer, and CTAB (cetyl trimethylammonium bromide) as a stabilizer; while, the reaction duration and temperature were adjusted to obtain palladium nanoarchitectures with different geometry [42, 43]. Tang et al. synthesized nanosheet-like palladium nanoarchitectures using $Pd(acac)_2$ (Pd(II) acetylacetonate) as a source of ingraining, PVP (poly-vinylpyrrolidone) as protecting agent, and NaBr as a reducer [44].

The exploitation of toxic reducers such as sodium borohydride or sodium bromide and non-biocompatible stabilizing agents, such as CTAB, is serious disadvantages of the previously mentioned chemical approaches for synthesis of palladium nanoarchitectures. Plasma synthetic approaches (atmospheric pressure (AP) alcohol cold plasma [45] & dielectric barrier discharge plasma [46]) have were investigated for clustering of palladium nanoarchitectures and other metallic nanoparticles. The AP alcohol plasma is characterized as a simple, environment friendly, and efficient technique for synthesizing small sized metallic nanostructures with interchangeable crystallization and crystal face [46]. Dielectric barrier discharge plasma is also ascribed as a highly efficient and time saving process for production of very fine and surfactant-free nanostructures [46]. With the advantages plasma synthetic approaches, more comprehensive researching reports are required for studying the applicability of these methods in nucleation of biomedical-palladium nanoarchitectures.

Biogenic synthetic approaches for clustering of biomedical- palladium nanoarchitectures, were found to be advantageous with needless of toxic synthetic reagents (solvents, reducing agents, and stabilizers), whereas, palladium nanoarchitectures could be nucleated from biogenic sources (like; plant-extracts, bacteria, alga, fungi, viruses, etc). The clustered palladium nanoarchitectures through biogenic techniques of synthesis are advantageous also with biocompatibility and stable dispersibility in biological environments. The exploitation of plant-extracts for clustering of biocompatible metallic nanostructures were reported to be the common approach of synthesis. The ingredients of the plant-extracts act the concurrent role of a reducing and a stabilizing agent. In particular, palladium nanoarchitectures, that were produced using white tea (Camellia sinensis) extract contained phenols and flavonoids, were exhibited with spherical shape and size distribution of 6-8 nm. Therefore, the as-produced palladium nanoarchitectures were successfully applied as antioxidant, antibacterial, and antiproliferative laborer for human leukemia [32]. Palladium nanoarchitectures that were prepared using Diospyros kaki leaves, were exhibited with size distribution of 50-120 nm and exhibited strong bactericidal action on *Escherichia coli and Staphylococcus aureus*. Porous palladium nanoarchitectures with rough protuberances that were ingrained using the extract of chaga mushroom (Inonotus obliquus) [34], showed to retain the anticancer action of chaga mushroom and showed an absorption band in NIR reagent. Therefore, it found to be successfully applied for anticancer therapies.

Size of palladium nanoarchitectures were shown to be more controllable via the chemical synthetic route rather than the biogenic approaches. By controlling reaction temperature, duration, or the concentrations of source of ingraining and reducer, palladium nanoarchitectures with a wide range of size averages could be produced. For instance, monodispersed palladium nanoarchitectures can be accurately prepared with size distribution of 5-10 nm by monitoring and adjusting the growing duration [47]. In another report, Size of mesoporous palladium nanoarchitectures was adjusted to be 25-42 nm via the application of cationic stabilizer and triblock copolymers [48]. In more recent, another approach investigated a green and simple technique for preparation of porous flower-shaped palladium nanoarchitectures with controllable size [28]. Whereas, size distribution of the prepared

nanostructures was 25-150 nm by controlling the chitosan concentration to act as a size-controllable laborer.

3. Palladium nanoarchitectures in photo-thermal therapy

Photo-thermal therapy (PTT) is extensively attracted the attention, because of its potential within the treatment of cancer and infection [49, 50]. This treatment uses light absorbers that convert photon energy into heat in order to thermally eradicate cancer and bacterial cells. So, utilize of the external laser irradiation with a controllable dose and beam diameter enables PTT therapy to be a selective and non-invasive treatment. PTT can eradicate the first tumour or metastasis tumour of the different cancer cells. Owing to the benefits of PTT, several researching groups focused on developing new promising nanomaterials for the PTT. Among these mentioned works, the research approaches interested in synthesis and application of metallic nanostructures as a promising candidate for image absorption due to the resonance of localized surface plasmon peak [51]. The ideal photo-thermal agent should be importantly characterized by, disperseability in water, shape uniform, small in size, near-infrared (NIR) absorption, high photo-stability, biocompatibility, targeting to bacteria/cancer cells and easiness to be excreted from renal system [52].

The photo-absorbers were needed to possess the strong absorption within the NIR region, which is an “optical window” with rock bottom light absorption and scattering of tissue; while, the absorbed light can deeply penetrate into the tissue [53]. Recently palladium nanoarchitectures were recently investigated to be applicable in this purpose. Palladium nanoarchitectures are emerging as an effective photo-thermal agent for PTT, attributing to their high-profile optical conversion efficiency, optical stability, variety in shape and size and high absorption in NIR region. Temperature of 27 ppm Pd nano-sheet solution was elevated from 28 °C to 48.7 °C after irradiation (808 nm, 1 W) to 10 min; while, the solution temperature was increased by 0.5 °C only. Small sized Pd nano-sheets (SPNS) was modified by reduction using glutathione (GSH) to enhance the prolongation of blood circulation, which facilitates the building up of nanomaterials within the tumour via improving the permeability and retention effect [44].

To enhance investigation of the target tumour, SPNS was modified by polyethylene amine (PEI). The trial in tumour-bearing mice showed good results with complete eradication of the tumour. Interestingly, GSH-Pd nano-sheet is often easily cleared from human body via the renal excretion path and going into the urine. Smalled size porous Palladium nanoarchitectures were recently reported, and found to be attractive photo-absorbers owing to their high photo-thermal conversion (93.4%) efficiency [37]. In 2018, Palladium nanoarchitectures was coated by chitosan oligosaccharide and then functionalized for the first time with the RGD peptide for PAI and PTT.

The biocompatibility of palladium nanoarchitectures was promoted by chitosan and therefore the RGD peptide enhanced the nanopalladium accumulation in the carcinoma cells of MDA-MB-231. Thus, great results on the in-vivo experiment were achieved by using a tumour-bearing rat model with injection. Within 20 days, the destroyed tumour was thermally reduced and fully cured without any side effects. However, multi-antibiotic resistance becomes a serious problem in modern medicine. Thus, the planning of new therapy for the infection treatment is a crucial. In 2019, another researching group developed the photo-thermal responsive membrane for the effective treatment of wounds [54]. Attributing to the significant photo-thermal behaviour of palladium nanoarchitectures, it was selected as a photo-thermal agent for inclusion in the photo-thermal-responsive membrane based on chitosan/polyvinyl alcohol. The advanced membrane showed high porous structure with an excellent biocompatibility, high swelling degree, high photo-thermal performance and high retention of moisture.

The test of in-vitro was furtherly demonstrated that the obtained membranes capable for killing E. coli bacteria using palladium nanoarchitectures (808 nm) under the effect of laser irradiation. So, it could be concluded that, owing to their biocompatibility, photo-stability, high absorption within the NIR region, high photo-thermal conversion efficiency and size/shape diversion, also as cost-effectiveness, palladium nanoarchitectures could be considered as promising candidates for therapy of cancer and infection photo-thermal.

4. Palladium nanoarchitectures in photoacoustic imaging

Recently, the molecular imaging techniques became interesting tools for the earlier remarking with accurate diagnosis, and enhancing serious disease treatment [40]. Photoacoustic Imaging (PAI) was recently developed as a completely unique promising imaging method for early cancer diagnosis. For enhancing the PAI contrast, the PA agents like nanoarchitectures are used [29]. Also, the PA agents (absorb in the NIR range) are normally utilized in the PAI because they easily penetrate for long depth in the biological cells. Stable with an efficient contrast is quite required for PAI. Nanostructures from gold were used as a PA agent, while some works demonstrated that the gold nano-stuctures are demolished after the irradiation for long-time by laser [29]. For example, the photo-thermal stability test exhibited that the gold nano-rod structure destroyed and quickly aggregated after 5 min under laser irradiation at an influence density of 80 mW/cm^2 [55]. While, the potential of palladium nanoarchitectures as PA agents didn't studied until Nie et al. reported an approach for the application of Pd nano-scaled structures as PAI based system, that displayed a highly stable and efficient audio-signal. to acquire the PA signal from the tumour was 3.5 times higher than the primary signal and reached a steady level thereafter 24 h in the meantime, while the control group (phosphate saline solution) showed quite weak signal for 24 h [55]. The cytotoxicity study of palladium based PAI systems during a mouse model evidenced that the main organs of the treated mice didn't noticeable damaged. The proposed Pd-based PAI is extremely promising for earlier detection of tumours. In 2018, a researching group reported that, chitosan polysaccharide-coated Palladium nanoarchitectures, which was recruited with RGD for targeted cancer cells (Pd@COS-RGD) as potent PA agents [56]. So, it acquired the tumour imaging after the injection with Pd@COS-RGD via the PAI system, while, the high accumulation of Pd@COS-RGD within the tumour region facilitated the assembly of a transparent image of the tumour tissue by the PAI system.

With the ability of active targeting, palladium nanoarchitectures are a great contrast agent for PAI, while, palladium nanoarchitectures often combined with other materials to make multimedia imaging for a high degree of sophistication in imaging techniques. As an example, Pd nanoarchitectures were coated with gold to make the core coat Pd@Au nano-plates (about 15 nm in diameter and 1.8 nm thick) for PAI and are calculated as tomography applications. When, PA imaging and CT imaging 24 h after Pd @ Au nanoparticle injection clearly demonstrated murine tumorigenesis. So, the presented study affirmed that, Pd@Au nanoarchitectures have the PA imaging and computed tomography in early cancer detection and management.

5. Palladium nanoarchitectures in antibacterial therapy

The antibacterial property of palladium nanoarchitectures was recently detected and the reported data exhibited palladium nanoarchitectures have high activity for antimicrobial applications. The antibacterial mechanism of palladium nanoarchitectures included both physical and chemical phenotypes. Hence, the facet of a Pd nanocrystal is in a position to disrupt the membranes of microorganisms [56]. As suggested in **Figure 2**, palladium nanoarchitectures are able to produce reactive oxygen species (ROS), which can cause the damage of cell wall & DNA, denaturation of protein and electron transport interruption, leading to the bacterial death [57]. The experimental results showed that the anti-pathogenic activity of palladium nanoarchitectures is best than that of Pd^{2+} ions [56]. The antimicrobial effect of palladium nanoarchitectures depends strongly on their size and shape. Ultrafine palladium nanoarchitectures with a 1 nm difference in size showed that the smaller palladium nanoarchitectures were more toxic to E.coli than large, and thus very small palladium nanoarchitectures showed a high antimicrobial effect even at very low concentrations (10−9 M) [56]. So, Pd nanocrystals of two different shapes (i.e., Pd cubes and octahedral Pd) showed antibacterial reactivity on both of gm-negative and gm-positive bacteria [57]. And, the face-dependent oxidase and peroxidase-like activities of the Pd nanocrystal have an excellent performance. Anti-bacterial properties by generating ROS to the gm-positive bacteria, the faceted cubic Pd have a simpler killing ability than the octahedrons Pd. While, the octahedrons can successfully penetrate into the membrane of gm-negative bacteria during a higher number than Pd nano-cubes, thus leading to higher antibacterial potency [57].

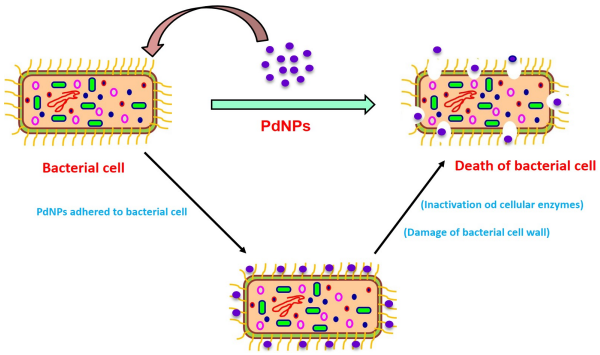

Figure 2: Applications of palladium nanoarchitectures in antimicrobial.

Palladium nanoarchitectures which were prepared by the biogenic methods, which showed a superior antibacterial property. For example, palladium nanoarchitectures, which were synthesized with biomass waste from Moringa oleifera petals such as a natural reducing and covering agent, showed an excellent antibacterial activity against Enterococcus faecalis [55]. Palladium nanoarchitectures, which were synthesized via green method using white tea extract (labelled Pd@W.tea NPs), also showed good antibacterial activity [29]. The experimental results on E. coli and Staphylococcus epidermidis declared that Pd@W.tea NPs have a far better antibacterial activity than white tea extract, possibly thanks to the strong force of Pd@W.tea NPs to the bacteria. On the other hand, the combination of Palladium nanoarchitectures with other metals might give a substantial composite with good antibacterial properties.

6. Palladium nanoarchitectures in antitumor therapy

Besides the antibacterial activity, palladium nanoarchitectures even have toxicity to the neoplastic cell line. The antitumor mechanism of palladium nanoarchitectures (**Figure 3**) including the physicochemical interactions of palladium nanoarchitectures with the protein functional groups such as phosphate groups and N- bases [58], the leakage of lactate dehydrogenase (LDH) [59], the generation of free radicals [60], and therefore the disturbance of the cell cycle [61]. DNA and proteins could transfer to inactive states through interaction with Pd nanoarchitectures. LDH plays an essential role in the production of usable energy for the cells. The LDH levels are often increased in most of cancer cell types [62], and therefore the leakage of LDH causes a significant problem to any functions of cancer cells. Incorporation of reactive nitrogen species (RNS) and reactive oxygen species (ROS) generates free radicals which causes the damaging in DNA, protein and lipid peroxidation reaction [63]. Till now, only a few studies have discovered the anti-tumour effect of palladium nanoarchitectures. In 2014, Balbín et al. report the initial evaluation of the anticancer activity of palladium nanoarchitectures in human cancer cells [64]. The apoptosis induction and G2/M cell-cycle disturbances on leukaemia cells suggested the anticancer cell effects of Pd nanoarchitectures [29]. Moreover, palladium nanoarchitectures which were prepared by using biomass waste from Moringa oleifera applied as naturally reducing and bio-capping agents. So, The MTT test on the human lung cancer cells (A549) and peripheral lymphocytes of normal cells showed the potential for further anticancer activities via tumour cell lines [55]. Palladium nanoarchitectures were obtained by employing a plant extract of Bauhinia variegate and showed anti-proliferative efficiency against the breast cancer (MCF-7) cells with quite low IC50 value (41.37 mg/L).

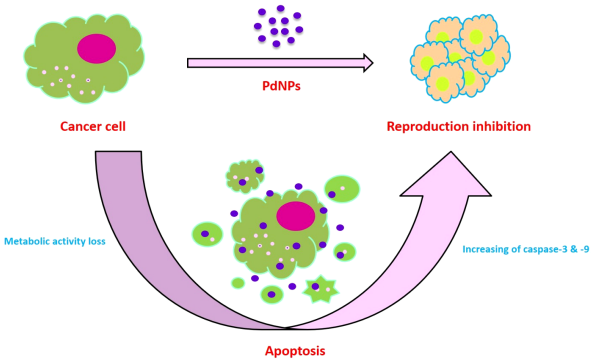

Figure 3: Applications of palladium nanoarchitectures in anticancer therapy.

7. Palladium nanoarchitectures in gene and drug delivery

In order to overcome the limitations inherent in conventional pharmacotherapy which presented in the low selectivity, severe toxicity and rapid excretion, a controlled drug delivery system was of interesting [65]. Therefore, nanoarchitectures can be performed to carry genes and drugs with a controllable targeting

ability. The drug particles can be loaded directly onto the pores of the nanoarchitectures or indirectly conjugated with the nanoarchitectures by a connected molecule. The high porosity of palladium nanoarchitectures was a superior property of loading both of drugs and genes. In comparison with porous AuNPs & porous PtNPs, the porous palladium nanoarchitectures exhibited quite better performance in the loading and release of gene [35]. For example, porous palladium nanoarchitectures synthesized with Chaga aqueous fungus extract can carry the drug through the electrostatic interaction between the cancer drug and the absorption molecules on the surface of nanoarchitectures [34]. The cancer drug was completely loaded within 6 h of incubation in the ambient conditions. The acidic pH (5.6) environment of the tumour tissue or cell lysozyme can allow more than 92% of drug to release which is significantly higher than at the neutral environment (30%) [34].

The therapeutic drug can also be indirectly coupled to palladium nanoarchitectures through a linker molecule. For example, the cancer drug, which was affixed to PEGylated palladium nanoarchitectures via a hydrazine bond, demonstrated a pH-responsive behaviour in the human cervical cancer (HeLa) cells and strong antineoplastic efficacy against helioma xenograft models in vivo [66]. Moreover, palladium nanoarchitectures have anti-cancer activity on many cancer cell lines, which leaded to on potential toxicity, which may influence the results of drug delivery behaviour. For the anti-tumour effects, the target cells/tumours should be carefully evaluated for cytotoxins of monorodic palladium nanoarchitectures those drug-loaded palladium nanoarchitectures for bimodal cancer.

The experiment of in-vitro displayed that 20 μg/mL of palladium nanoarchitectures, which was synthesized with chaga mushroom extract, were ready to kill ≈ 20% of HeLa cells. While, 30% of the HeLa cells were reduced by the cancer drug-laden palladium nanoarchitectures (20 μg/mL of Pd) [34]. Nevertheless, this issue wasn't considered in many reports, for instance , the effect of palladium nanoarchitectures alone on Hela cells wasn't tested in literature [34]. To detect the successful delivery of drug/gene to the targeting tissues, palladium nanoarchitectures concentration at which it doesn't cause the poisoning to the non-targeted tissue must be tested. The laboratory cell viability assay showed that palladium nanoarchitectures are porous to a degree of up to 0.5 eq. offered cytotoxicity that can be ignored for NS3-Huh7 cells (human hepatitis C-borne liver cancer cells) and non-structural protein (3-silicon). Therefore, the concentration of palladium nanoarchitectures at 0.5 is equivalent and often used in drug/gene delivery studies.

8. Palladium nanoarchitectures in prodrug activation and transformation processes

Bio-orthogonal reactions allow the formation or splitting of the chemical bonds in a specific locus of the medical molecules within the physiological environment. These reactions are useful for marking, tracking, activating, transforming and manipulating medicinal particles. Usually, bio-orthogonal reactions are applied to activate the nontoxic precursor to the toxic drug and reducing the side effects for treatment of cancer. Support unique motivational characters and biocompatibility for palladium nanoarchitectures, the Pd-mediated stimulation reaction might enable activation of the prodrugs. The cancer drug of 5-fluorouracil (5FU) was developed about 50 years ago but still the toxicity has some limiting due to its clinical efficacy [67]. The heterogeneous Pd^0 was ready to catalyse the nontoxic precursor at the extracellular level, and was recently developed to scale back the systematic toxicity of 5FU. Moreover, the heterogeneous Pd^0 catalysed a biologically inert precursor through functionalization on the N1 position. As an example, the heterogeneous Pd^0 catalysed biologically inert precursors to the cytotoxic gemcitabine. Considering with the assembly and / or passivation of palladium nanoarchitectures into biological media, Pd-based nanostructures must be developed. Palladium nanoarchitectures coated in a porous silica shell were developed in order to remove the pd-stimulated wrinkles and Suzuki-Miyaura intermolecular connections in aqueous media related to biosynthesis [68]. Therefore, the chemical interaction management in the living systems may be a difficult issue. In order to mimic the allosteric regulation mechanism for the bi-enzymes, the controlling in bio-orthogonal catalyst was improved [69]. By changing the structure induced by light, the catalytic reaction is often regulated. Versatile and adaptable Pd-based orthogonal bio-stimulants are often used in a variety of chemical reactions in the living cells for ultra-precise imaging and treatment.

9. Palladium nanoarchitectures in biosensing

Biosensors are devices that use high-quality biological reactions for detection of target analytical materials. The first issue in a biosensing is the biosensor, which provides a link to a specific analytes and the second issue is the physical transformer that is responsible for translating the dynamic reaction into a measurable effect (i.e. optical emission, electrical signal and mechanical motion) [70]. Dopamine (DA) is crucial catecholamine neurotransmitter and therefore the detection of DA is important for the first diagnosis and subsequently prevention of some diseases, such as Alzheimer, Parkinson as well as schizophrenia. Due to the formidable electro-catalytic detection of DA, Yi et al. immobilized palladium nanoarchitectures into nano-porous gold (NPG) to design the DA biosensor. The combination of the electrical stimulation effects of Pd of DA sensor with the two-dimensional nanostructure of the NPG wire considerably improved the response current also due to the signals of electrochemical. Owing to the high sensitivity, wide detection range and excellent selectivity, this sensor is significantly promising for DA-tracked detection. This demonstrated that the nanostructure can improve the performance of biosensors [71], therefore, Soleymani et al. reported that, the device architecture consisting of a widely ranged of nanostructure to show the response of different sensors (**Figure 4**) [72]. Employing of metal electrodeposition with different plating conditions leaded to generation of a nanostructured Pd electrodes to complete the microelectrode array. The high binding affinity of Pd with thiols allowed the functionalization and linked bio-molecular probes with the nanostructured microelectrodes. The excellent performance of nano-scaled biosensors is significantly promising for the development of high-achievement diagnostic tools in the purposes of medicine.

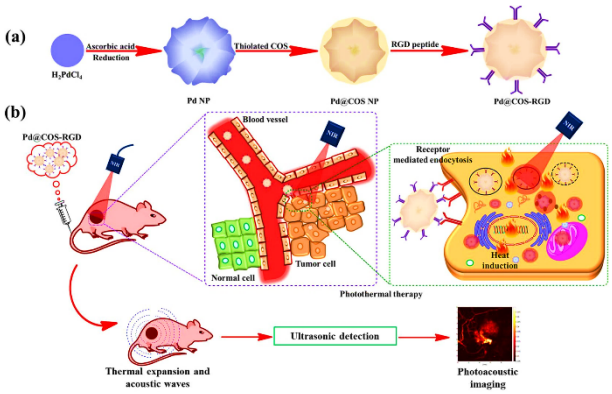

Figure 4: Schematic for applications of palladium nanoarchitectures in biosensing (Nature permission, open access license) **[12]**.

10. Conclusion

Palladium nanoarchitectures are advantageous with superior catalytic and optical activities. But, till now, very few researching reports were taken the advantage of these unique properties for its applicability in the biomedical purpose. This review acts in motivation for sharing up-to-date information on the potentiality of palladium nanoarchitectures in the biomedical purposes. The most recent reports on the applicability of palladium nanoarchitectures for infection/cancer PTT, photoacoustic imaging, bactericidal applicability, antitumor therapy, drug and gene delivery, prodrug activator, biosensor, and multifunctional nanostructures are extensively reported. The overview of toxic effects, pharmacokinetic, and bio distribution of palladium nanoarchitectures was demonstrated. Eventually, a perceptual sign is represented for the future of exploitation of palladium nanoarchitectures in biomedical purposes.

Conflicts of interest

Author declares that he has no conflict of interest

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