reduces the ability of passive targeting as well as shortening the shelf life of nanoparticles in the bloodstream [89].

Comparison of passive targeting of small molecules IRDye 800CW and GSH-coated luminescent gold nanoparticles in vivo showed that the nanoparticles are similar to dye molecules in early physiological stability and clearance from kidney. However, GSH-coated gold nanoparticles showed much longer tumor retention time than dye molecules. It was observed that the nanoparticles were cleared from healthy tissues approximately threefold faster than the dye molecules (Fig. 12) [90]. A number of active and passive targeting studies discussed in this chapter are summarized in Table 1.

4. COMPARISON OF ACTIVE AND PASSIVE TARGETING

It has been proven that the difference between targeting strategies determined the outcomes and therapeutic efficacy of the established formulation. In this regard, two polymeric nanoparticles were synthesized and then peptide GE11 (for active epidermal growth factor receptor targeting) was attached to one of them and no agent was attached to the other and studied as passive targeting. It was shown that nanoparticles functionalized with GE11 peptide that specifically enter the target cells resulted in better therapeutic outcomes than passive targeting, indicating the high efficacy of active targeting compared to the passive targeting (Fig. 13) [91].

In an attempt, the efficiency of active targeting [by Arg-Gly-Asp (RGD) and Asn-Gly-Arg (NGR) peptides] was compared with passive targeting (by EPR effect). It was observed that after injection into tumor-bearing mice, passive targeting resulted in more accumulation in the tumor than active targeting. The results indicate that active targeting should not always be considered superior and more efficient than passive targeting (Fig. 14) [92].

Also in another attempt, passive targeting (by EPR effect), active targeting (by RGD peptide for αvβ3 integrin targeting), magnetic targeting by magnetic field placed in the tumor region, and also combined of active targeting with magnetic targeting were compared in terms of therapeutic efficacy, efficacy as contrast agent for MRI imaging, as well as ex vivo biodistribution using PLGA-based nanoparticles loaded with PTX and superparamagnetic iron oxide (SPIO) was evaluated. It was found that the combination of active targeting with magnetic targeting resulted in an eightfold increase in drug accumulation in the tumor area compared with passive targeting. It was observed that the therapeutic efficacy and the MRI contrast ability in combination method were increased compared with passive targeting or single targeting mode (Fig. 15) [93].

HPMA copolymer-docetaxel and HPMA copolymer-docetaxel-RGDfK complexes were also evaluated to target cancer cells [94]. Hui et al. synthesized liquid-filled silica nanocapsules with a range of hardnesses and found that there is a relation between the hardness of

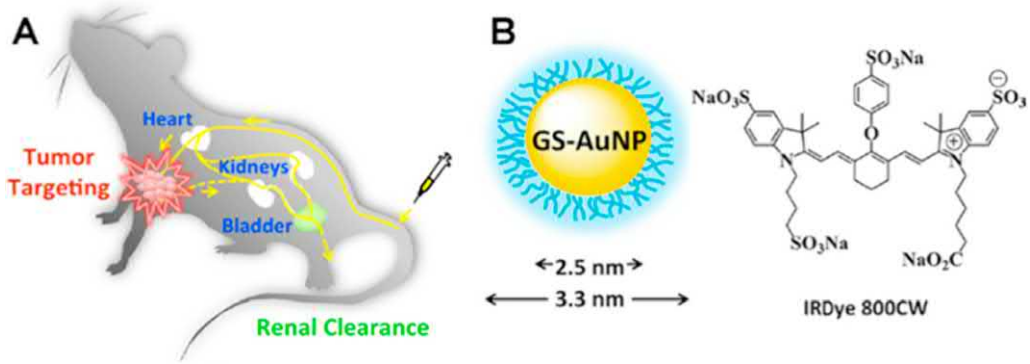

FIG. 12 (A) Schematic illustration of tumor targeting and (B) IRDye 800CW structure and glutathione-coated luminescent gold nanoparticles. (Reprinted from J. Liu, et al., Passive tumor targeting of renal-clearable luminescent gold nanoparticles: long tumor retention and fast normal tissue clearance, J. Am. Chem. Soc. 135 (13) (2013) 4978–4981 with permission from American Chemical Society.)