measured. The molecular docking data exhibited that aflatoxin G1 and B1 were bound onto IB subdomain in HSA predominantly through hydrogen bonds and hydrophobic interactions and these results were well matched to the fluorescence spectra. The interaction constants attained by the docking studies were matched to those of the experimental values measured from the fluorescence spectra compared with those achieved by the MD simulations. Overall, the results obtained from the MD simulations molecular docking and fluorescence spectra confirmed each other.

It is found that the crystallization capacities of proteins are enhanced on substituting lysine residues in their surfaces by other residues. Matrix-assisted laser desorption and ionization time-of-flight mass spectra were acquired experimentally for the PH1033 protein of *Pyrococcus horikoshii* that was chemically modified by NHS-biotin to assess the surface lysine residues [111]. The biotinylation of protein using 1:1 molar ratio indicated that merely 7 of 22 lysine residues existing within the protein containing 144 residues were biotinylated. MD simulations were done to mimic and analyze the experimental results confirming the biotinylation was considerably affected by four parameters related to the local surroundings of lysine residues including pK_a values, solvent accessibility, number of hydrogen bonds, and electrostatic energy. Therefore the biotin functionalization avoids using lysine residues having high intramolecular interactions that can decrease the proteins crystallinities.

9. NANOPARTICLES AS DRUG DELIVERY SYSTEMS

Nanoparticles with small diameters in the 10–100 nm range can be served as effective drug carriers that are freely circulated even in capillaries thus they are naturally superior compared with bigger drug transporter materials in crossing some biological barriers [112]. It is worth mentioning that, nevertheless, nanomedicines pass longer and more difficult FDA approval processes relative to parent unimolecular drugs [113]. The reason is that it is required to investigate the effectiveness, side effects, in vivo aggregation, drug release, and other properties of nanomedicines each components of their formulations to be FDA-approved as nanocarriers. FDA regulations, nanocarriers complexity and performance changes by reformulation of small drugs into the nanocarriers/nanomedicines are among important issues for the nanocarriers commercialization by the pharmaceutical companies. Fortunately, as the number of FDA-approved drugs and those currently used in clinics is increasing [114, 115] and FDA presents more obvious nanomedicine approval rules, there is a growing interest in clinical nanomedicine development [113].

The PEG amount and temperature effects on the PEGylated NPs translocation through the asymmetric plasma membrane in eukaryotic cells were examined by coarse-grained MD simulations [116]. It was exhibited that NPs translocation in the membranes was enhanced by raising the temperature and this was related to formations of more disordered lipids and quicker diffusion. In contrast, steric hindrance influence by PEG inhibited the NPs translocation and promoted flip-flop of lipids. The PEG chains were rearranged to decrease the interactions of lipid tails and PEG throughout the translocation and this looked like the snorkeling. Besides, flip-flops of lipids were changed with the PEGylation degree and the translocation direction by the NPs. Greater amount of PEGylation promoted the flip-flops of lipids whereas it inhibited the extraction of lipids from bilayers. More symmetric membranes were created on lipids extraction and their flip-flops.

Oral chemotherapy method is favored over injection and other methods nevertheless its usage is limited as anticancer drugs reveal little bioavailability [117]. Self-assembled nanoparticles can be applied as promising nanocarriers to solve this issue however designing suitable nanocarriers is challenging. Effective DDSs of HA (hyaluronic acid) copolymers were designed for the DOX drug using MD simulations and the chain length effect in the fatty glyceride of HA was estimated on peroral DOX absorption. MD simulations were done to assess the DOX compatibility with HGS (HA-*g*-glyceryl monostearate), HGL (HA-*g*-glyceryl monolaurate), and HGC (HA-*g*-glyceryl monocaprylate). The HA copolymers were also synthesized to confirm the predicted results. The HGS, among all copolymers, exhibited the most compatibility by DOX and then HGL and HGC. The stability and physicochemical features of all nanoparticles were dependent on the structures of copolymers so that the HGS/DOX nanoparticles displayed superior characteristics and subsequently HGL/DOX and HGC/DOX nanoparticles. This trend was observed for the epithelial transport, cellular uptake, and in vivo absorption tests in rats as HGS/DOX NPs revealed seven times greater absorption when perorally administered compared with the intravenous DOX injection. Hence the MD simulations effectively used to rationally design nanoparticles for the oral transport of DOX.

Drug carriers based on lipids are auspicious materials for hydrophobic drugs. Distribution of lipids in droplets changes their loading capacities. Consequently, MD simulations were performed on diverse kinds of lipid