RNA nanoclusters were constructed using some nanorings with sizes of up to 20 nm and their structural characteristics were studied by MD simulations under physiological human body conditions used to deliver drugs [94]. The variations of ion concentrations about RNA nanoclusters were examined by changing temperature and time. It was revealed that raising the temperature increased the number of ions at a distance from the nanotube but the number of ions decreased at this distance nearby the nanoclusters by quenching the simulations. Thus it was found that some ions evaporated on decreasing the temperature and this happened for the nanorings. The RDF data demonstrated a result comparable with the temperature that was obtained for the RNA nanoring.

MD simulations were accomplished using empirical force fields in solution to get insights about the dynamical and structural characteristics of RNA and DNA [95]. One RNA and three DNA sequences were simulated by CHARMM27 all-atom force field designed for the nucleic acids to examine their dynamical, structural, and hydration features such as helical distributions, sugar puckering, and dihedral angles. As well, canonical B and A forms of a DNA hexamer in 75% and 0% ethanol were simulated. The differences in root mean squares of the canonical B and A forms of DNA showed that they had extremely different behaviors confirming such force field could examine the equilibrium state for the two DNA forms. High stability of A form in 75% ethanol but B form in water displayed that the equilibrium was changed through factors such as solvent. Therefore this force field could successfully reproduce various experimental results for the RNA and DNA duplex approving it was very useful for application in computational studies on nucleic acids and their interactions by lipids and proteins.

MicroRNAs are noncoding RNAs that can regulate gene expressions within biological systems. In many diseases such as cancer extensive deregulation of miRNAs happened so that some miRNAs become oncogenes and/or tumor-suppressive materials by concurrently targeting various mRNAs. Accordingly, miRNAs are used as auspicious therapeutics in cancer therapies. In this context, peptide nucleic acids (PNAs) were designed that could target 3′UTR over the MYCN mRNA and sis not contain complete complementary base pair sequence, similar to miRNAs. In these experiments, miRNA-34a was chosen as the model that could suppress tumors in numerous cancer cells such as neuroblastoma. Particularly, the miRNA-34a could directly regulate the MYCN oncogene as its overexpression was used as a beneficial biomarker in extremely aggressive phenotype of neuroblastoma. Three oligomers of PNA with diverse lengths were designed, synthesized and their interactions by two binding domains onto the MYCN mRNA target were examined through MD simulations, ultraviolet-visible and circular dichroism spectra [96]. Uptake in vitro tests and confocal microscopy images for the PNA sequences were acquired using neuroblastoma Kelly cells. Interestingly, although the RNA/PNA hetero duplexes had several mismatches, they highly retained their cellular uptake, affinity, and stability.

7. PEPTIDES AND CELL PENETRATING PEPTIDES AS DRUG DELIVERY SYSTEMS

Peptides are short chains formed from amino acids that are bound through peptide bonds [97]. They involve in numerous key biological processes and form precise secondary structures and nanomaterials indicating controlled properties. Nanostructured peptides exhibit outstanding characteristics as they are biodegradable, versatile, bioactive, and biocompatible [98]. Hence, they are used in biomedicine particularly in tissue engineering, drug carriers, and antimicrobial agents.

Efficient therapeutic transport in the plasma membrane of cells can be a problem mainly for therapeutics that are large, ionized, or strongly linked onto the proteins in plasma [18]. Cell penetrating peptides (CPPs) were introduced in 1994 as drug carriers for application in intracellular transport of drugs [99]. It was found that the CPPs interactions with cell membranes occurred through electrostatic contacts with proteoglycans. Also the cellular uptakes of CPPs were influenced by factors such as cell type, the secondary and the primary CPPs structures, membrane composition, cargo nature/concentration, concentrations of salts, and CPPs. As CPP-cargo conjugates and CPPs can internalize by endocytosis pathway, an effective way for the delivery of cargo-CPP is the endosomal escape [100]. Both of the covalent and noncovalent bonds can be formed between CPPs and pharmaceuticals to form DDSs.

MD simulations were carried out on the formation of polypeptide membranes from surfactant resembling peptides containing 15 amino acids that created a hydrophobic domain including three valines (V), three isoleucines (I), three glycines (G), three alanines (A), and a hydrophilic area generated through three lysines (K) [101]. Figs. 17 and 18 illustrate the initial and final structures of the $K_3G_3A_3V_3I_3$ and $I_3V_3A_3G_3K_3$ polypeptides. The density values, hydrogen bonds amounts, van der Waals and Coulombic interactions among peptide-peptide residues and peptide-water specified that although much water was infiltrated, the membranes maintained their structures.