

result in wound dehydration and bacteria invasion and a sublayer with high absorption capacity and antibacterial properties. It was prepared from poly(caprolactone) and poly(vinyl acetate) and loaded with carvacrol. The drug efficiencies were in the range of 40%–50%. Significant inhibition of Gram-negative (*E. coli* S17) and Gram-positive (*S. aureus* ATCC 25923) bacteria growth clearly revealed the potential of the membranes in wound healing. Cytocompatibility studies further revealed that the membranes were cytocompatible and the cell migration was not hindered by the release of carvacrol from the membranes [119]. Fahmy et al. prepared cross-linked poly(vinyl alcohol)-hyaluronic acid membranes composed of varied amounts of hyaluronic acid via freeze-thawing method. The membrane was loaded with ampicillin. The membrane exhibited good swelling capability, mechanical flexibility, and protein adsorption. Membranes with hyaluronic acid content less than 20% displayed high cell viability with the absence of toxic effect in vitro. The drug loaded membrane exhibited antimicrobial activity against *S. aureus*. The membrane which was not loaded with a drug was effective against *Candida albicans* which is attributed to the presence of hyaluronic acid used for the development of the membrane [120].

Cheng et al. developed collagen, polytetrafluoroethylene, and glycolide fiber membranes which were loaded with either amoxicillin or tetracycline. The adhesion of *Aggregatibacter actinomycetemcomitans* and *Streptococcus mutans* into the membranes loaded with or without the antibiotics was studied. The bacteria attachment on collagen membranes was high when compared with polytetrafluoroethylene and glycolide fiber membranes which were not loaded with antibiotics. However, the incorporation of tetracycline or amoxicillin significantly reduced the adhesion of bacteria to the membranes. The findings confirmed the efficacy of loading antibiotics to membranes used for biomedical applications [121]. El-Shinnawy et al. reported bacterial cellulose-based membrane loaded with gentamicin, ampicillin, and chloramphenicol at varied concentrations. The membrane loaded with chloramphenicol was active against all strains of bacteria used in the study. The membrane loaded with ampicillin was active against all the strain of bacteria except *S. aureus* and the membrane loaded with gentamicin membrane was active against *P. aeruginosa* and *B. subtilis*. In vivo studies in a rat model over a period of 14 days revealed reduced inflammation with enhanced wound healing and skin regeneration which was significant in the membrane loaded with gentamicin [122]. Brianezi et al. developed chitosan-methoxy polyethylene glycol-

poly(caprolactone) copolymer membranes loaded with gentamicin. The membranes exhibited reduced burst release effect with good swelling capability. The drug-loaded membranes were active against *S. aureus* and *E. coli* growth [123].

Rivero et al. developed pH-sensitive membranes loaded with nitrofurazone for wound dressing. It was prepared via electrospinning and the application of a pH-sensitive polymer made the membranes to release the drug in a pH greater than 7. The membranes selectively released the drug in a physiological pH of the wound that indicates signs of infection. The pH-dependent release capability of the membrane indicates that they are potential dressings for chronic wounds [124]. Shen et al. loaded chloramphenicol to porous SBA-15-cellulose membrane. The drug release from the membrane was sustained for 250 h and they were effective on *S. aureus* and *E. coli* for 144 h. The tensile strength, water vapor transmission rate, and swelling capability of the wound dressing were suitable for wound-healing application [125].

### 3.8. Polymer-Drug Conjugates

Polymer-drug conjugates are nanocarriers in which bioactive agents are conjugated to a polymer-based water-soluble carrier. Based on Ringsdorf model, polymer-drug conjugates are composed of a biocompatible polymeric carrier and low-molecular weight bioactive agents, which are conjugated by a bioresponsive linker to the carrier (Fig. 8). The conjugation of bioactive agents to the polymer offers several advantages such as improves the water solubility of the drug which are hydrophobic in nature, enhances the pharmacokinetic profile of the conjugated drug, extend the drug plasma half-life and volume of distribution; reduces clearance by the kidneys or liver; and protects the conjugated drug against degradation [126,127].

The functions of the linker used for the conjugation of drugs to polymers are for controlled and triggered drug release under selected pH and the presence of enzymes [128]. Targeting moiety and solubilizing unit are also incorporated into polymer-drug conjugates to enhance the therapeutic outcomes of the conjugates [129,130].

Shaunak et al. prepared hyperbranched dendrimers from anionic, polyamidoamine, generation 3.5 dendrimers incorporated with D(+)-glucosamine 6-sulfate and D(+)-glucosamine which are antiangiogenic and immuno-modulatory agents, respectively. The dendrimer glucosamine inhibited Toll-like receptor 4-mediated lipopolysaccharide-induced synthesis of