Table 3 Natural and synthetic biomaterials used in angiogenic growth factor delivery

Biomaterial	Properties	Applications	References
	Naturals		
Collagen/ gelatin	Important component of ECMs and forms thermally reversible gels; functionally important qualities such as adhesiveness for cells and proteolytic degradability are retained in gelatin	Porous interconnecting network for EC adhesion and migration, and collagen hydrogel for angiogenic GF release in a controlled manner	[104-106]
Fibrin	Sealing malleable matrix prepared from autologous plasma and available as glue or as engineered microbeads	Fibrin-based hydrogels can be surgically applied as sealant and adhesive in fibrin glue (mixture of concentrated fibrinogen and thrombin usually derived by cryoprecipitation of human plasma): useful as GF-controlled release systems to stimulate angiogenesis	[107-109,102,110]
Hyaluronic acid	Glycosaminoglycan present in the natural ECM and composed of repeating units of D-glucuronic acid and N-acetyl-D-glucosamine; HA forms hydrogels by various covalent cross-linking methods; high biocompatibility and biodegradability	Stimulation of *in vivo* angiogenesis by HA hydrogels loaded with GFs such as VEGF-A, bFGF and KGF	[111-113]
Alginate	Nontoxic polysaccharide-based polymer of marine origin with the fraction and sequence of the two monomers, α-L-guluronic and β-D-mannuronic acid sugar residues varying over a wide range; ECM-mimetic features, physical cross-linking, biocompatibility and erosion	Alginate microspheres, beads and hydrogels for angiogenic GF release	[114-121]
Chitosan	Polysaccharide with tunable chemistry that allows for the control of degradation properties; low cost and easily available biopolymer with structural similarity to natural glycosaminoglycans; temperature/pH-sensitive gels can formed from quaternized chitosan and glycerophosphate, and used as an intelligent carrier	Chitosan forms hydrogels by physical cross-linking or chemical cross-linking which can incorporate GFs such as FGF; useful scaffold for injectable biological materials	[122-124]
	Synthetics		
PLGA	Good biocompatibility, biodegradability, low immunogenicity, low toxicity and mechanical strength; FDA-approved polymer for drug delivery	PLGA microparticles and solid scaffolds as controlled delivery platforms for VEGF-A, IGF-I, TGF-β1 and other GFs	[125,90,126-130]
PEG-based synthetic biomaterial	Bioinert material explored as a non-degradable option in protein delivery; PEG can be readily conjugated with other natural and synthetic materials	PEG copolymers able to form environmentally sensitive hydrogels and to allow the attachment of biologically specific peptides to enhance control release of angiogenic GFs	[131-135]
Aminoacid-based polymers	Biodegradable materials that can be complexed with gelatin to prepare pH-sensitive matrices for controlled protein delivery	Poly(γ-glutamic acid)-sulfonate, gelatin-polylysine (gelatin-PLL) and gelatin-poly(glutamic acid) (gelatin-PLG) hydrogels for controlled delivery of FGF	[136,137]
Polyacrylamide and derivatives	Thermosensitive polymers that undergo phase transition near the body temperature	Steric stabilization of liposomes; useful to deliver VEGF to human vascular ECs over an extended time period	[138,139]