Table 1: Stimulators of Angiogenesis

Angiogenic Stimulator	Functions	Reference
VEGF	Inducer of angiogenesis and lymphangiogenesis.	34,35
FGF	Regulates endothelial cells proliferation, migration and differentiation.	35
HGF	Stimulates cell growth. Useful for the treatment of critical limb ischemia.	36
Ang1 and Ang2	Stimulates the matured vessel formation and regulate angiogenesis.	37
PDGF	Stimulates angiogenesis and regulate cell growth and division.	38
IGF	Stimulates angiogenesis and myogenesis and induces nerve regeneration.	39
Endoglin	Stimulates endothelial cell proliferation, extracellular matrix production and TGF-β/ALK1 signal transduction.	40
Interleukin 8	Stimulates endothelial cell proliferation, survival and matrix metalloproteinases.	41
Thyroxin	Stimulates early coronary angiogenesis.	42
VE-cadherin	Stimulates endothelial junctional molecules.	43
G-CSF	Helps in endothelial cell proliferation and act as neuro-protective agent.	44
Integrins	Promote cell attachment and stimulates cell migration.	45
Ephrin	Helps in vascular development and angiogenic remodeling also determine the formation of arteries or veins.	46
eNOS	Stimulates angiogenesis via eNOS signaling cascade.	47
TGFbeta	Induces angiogenesis through VEGF-mediated apoptosis. Plays a dual role as a tumor suppressor in early stages and as tumor promoter in late stages of tumor progression.	48, 49
YKL40	Angiogenic factor to promote tumor angiogenesis and plays role inradioresistance, and progression of glioblastoma.	50, 51
HIF1α	Regulate tumor angiogenesis and invasion.	52

HDGF	Plays vital roles in cancer cell transformation, angiogenesis, apoptosis and metastasis.	53
Notch/DLL4	Negative regulator of tumor angiogenesis and upregulated in tumor vasculature in cancer progression.	54, 55
Semaphorins	Anti-angiogenic agents, stimulate tumor angiogenesis.	56

Table 2: Anti-angiogenic drugs for the treatment of tumor

Anti-angiogenic Drugs	Mechanism of action	Cancer types	Ref.
Avastin	Anti-VEGF monoclonal antibody	Advanced metastatic colorectal cancer and glioblastoma.	75
Sunitinib	Act as multi-TKI that targets VEGFR-1–3, PDGFR.	Kidney cancer and neuroendocrine tumors	76,77
Sorafenib	TKI which targets VEGFR-2, -3, Flt-3 PDGFR-b.	Primary kidney cancer, RCC, liver cancer.	77,78
Everolimus	Inhibitor of mammalian target of rapamycin (mTOR)	Kidney cancer and neuroendocrine tumors	79
Imatinib	(TKI) Selective inhibitor of Bcr/Abl	CML and GIST.	80
Pazopanib	Act as multi-targeted receptor tyrosine kinase inhibitor	Kidney cancer and soft tissue sarcoma	81
Axitinib	Second generation inhibitor of VEGF-1, 2, and 3.	Renal cell carcinoma	82
Denibulin	Vascular-disrupting agent (VDA) and reversibly inhibits	Solid tumors	72

(MN-029)	microtubule assembly.		
ZD6126	Vascular targeting agent and VDA	Metastatic renal cell carcinoma and metastatic colorectal cancer	[73]
ABT-571	VDA and acts as antimitotic agent.	Non-small cell lung cancer	[71,83]
Ombrabulin (AVE8062)	VDA	Advanced-stage soft-tissue sarcoma and head and neck squamous cell carcinoma	[71,83]

Table 3: Anti-angiogenic nanomaterials and their therapeutic applications

Serial No.	Nature of nanoparticles	Anti-angiogenic activity	Ref.
1	Cerium oxide	Ovarian tumor model	[119]
2	Fullerenols (F) and its conjugates	Zebrafish and murine tumor angiogenesis models	[113]
3	Chitosan	Inhibition of hepatocellular carcinoma xenografts	[120]
4	Fullerenic	Inhibition of MCF-7 breast tumor model	[121]
5	Tetrac	Inhibition of Human Renal Cell Carcinoma Xenografts	[122]
6	Biosynthesized AgNPs	Anti-angiogenic activity	[123]
7	Carbon	Inhibition of glioblastoma multiforme	[124]
8	Gold	Anti-angiogenic activity in HUVEC	[125]
9	Gold	Anti-angiogenic activity in CAM model	[126]
10	Functional peptide With AuNPs	Inhibition of *in vitro* angiogenesis	[127]
11	GO & rGO	Switchable angiogenic and anti-angiogenic activity	[114]
12	Gold	Ovarian cancer in mouse model	[128]

13	Biogenic AgNPs	Anti-Angiogenesis effect on CAM	129
14	Cuprous oxide	Inhibition of angiogenesis via down regulation of VEGFR2 expression	130
15	Carbon nanomaterials: and its derivative.	Anti-angiogenic activity through the down-regulation of KDR	131
16	Silicate	Anti-angiogenic effect on retinal neovascularization	132
17	NAMI-A-loaded mesoporous silica	Inhibition of angiogenesis by the production of ROS	133
18	Perfluoro carbon	Diagnosis and treatment of atherosclerosis	134
19	Magnetic mesoporous silica-based siRNA	Orthotropic ovarian cancer therapy	135
20	Peptide	Anti-angiogenic therapy in glioma model	118
21	AuNPs & AgNPs with heparin	Inhibition of FGF2 induced angiogenesis	136
22	Gold	Anti-angiogenic activity through heparin-binding glycoproteins	137
23	Biosynthesized AgNPs	Inhibition of VEGF-and IL-1 - induced vascular permeability in PRECs	138
24	Perfluorocarbon	Anti-neovascular efficacy in the rabbitVx2 cancer model	139