ISSN : 0974 - 7508 Volume 9 Issue 7

Natural Products

An Indian Journal

Review

NPAIJ, 9(7), 2013 [294-297]

# Anti-angiogenic property of some plants

**Namrata H.Boghani, Meonis A.Pithawala***

**C.G.Bhakta Institute of Biotechnology, UKA TARSADIA UNIVERSITY, Gopal Vidyanagar, Bardoli Mahua Road, Tarsadi, 394350, (INDIA)**

**E-mail: namrata88boghani@yahoo.co.in; meonis_pithawala@yahoo.com**

## ABSTRACT

There is an increasing demand for the herbal drug treatment of various ailments and many plant drugs from Ayurvedic system are being explored globally. This article acts as a quick reference for extracting the anti-angiogenic properties of the following selected medicinal plants *Allium sativum, Aloe vera, Anacardium occidentale Linn, Ardisia pyramidalis (Cavanilles) Persoon, Bidens pilosa Linn., Boerhaavia diffusa, Bombax ceiba, Camellia sinensis, Clerodendrum serratum (spreng.), Coffea Arabica, Gardenia jasminoides, Glycyrrhiza glabra, Parkia speciosa, Salvia officinalis, Silybum marianum, Tillandsia recurvata L., Withania somnifera.* 

## KEYWORDS

Ayurveda;
Anti-angiogenic property;
Herbal drug.

## INTRODUCTION

Angiogenesis, the formation of new blood vessels from pre-existing capillaries and circulating endothelial precursors, plays a critical role in a various physiological and pathological processes such as embryonic development, wound healing, chronic inflammation, tumor growth, and metastasis[1-2]. Angiogenesis is regulated by numerous factors, such as vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), tumor necrosis factor-α (TNF-α), and interleukin-8 (IL-8)[3]. There are numerous bioactive plant compounds and dietary products that have been tested and are being tested for their anti-angiogenic potentials in search of proangiogenic anti-angiogenic drugs[4]. Some plants having anti-angiogenic properties are described below.

### Allium sativum (Garlic) family: Amaryllidaceae

Alliin, a compound derived from garlic, demonstrated dose-dependent inhibition of fibroblast growth factor-2 (FGF2)-induced human endothelial cell tube formation and angiogenesis in the chick chorioallantoic membrane (CAM) model[5]. Additionally, alliin demonstrated potent inhibition of vascular endothelial growth factor induced angiogenesis in the CAM model. The nitrogen oxide synthesis inhibitor nitro-L-arginine methyl ester (L-NAME) reversed the anti-angiogenesis efficacy of alliin in the CAM model. These data indicated a synergistic effect of antioxidants on the anti-angiogenesis and anticancer efficacy of alliin[5].

### Aloe vera (Aloe barbadensis) family: Xanthorrhoeaceae

Aloe-emodin (AE, a hydroxyanthraquinone from *Aloe vera* and other plants) identified as a new anti-angiogenic compound with inhibitory effects in an in vivo angiogenesis assay and evaluated its effects on specific key steps of the angiogenic process[6]. Two main targets of the pharmacological action of AE as an anti-angiogenic compound seem to be urokinase secretion and tubule formation of endothelial cells. These data

showed that AE can behave as an anti-angiogenic compound[6].

**Anacardium occidentale Linn. (Cashew) family: Anacardiaceae**

*Anacardium occidentale* extract was able to suppress VEGF-induced angiogenesis in vivo in the chorio allantoic membrane, rat cornea, and tumor induced angiogenesis in the peritoneum of EAT bearing mice[7]. The extract inhibited cell proliferation of different tumor cells such as EAT, BeWo, and MCF-7 in vitro in a dose-dependent manner and it reduced the VEGF level in the ascites of treated mice. A decrease in the microvessel density count and CD31 antigen staining of treated mice peritoneum provide further evidence of its anti-angiogenic activity. The VEGF system of angiogenesis is the molecular target for the anti-angiogenic action of AOE[7].

**Ardisia pyramidalis (Cavanilles) persoon family: Myrsinaceae**

The angiosuppressive activity of leaf extracts of *Ardisia pyramidalis* was determined using the duck in ovo chorioallantoic membrane (CAM) assay. The methanol extract was anti-angiogenic as indicated by the statistically significant lower blood vessel count compared with the negative control and the untreated eggs[8].

**Bidens pilosa Linn. (Spenish needle) family: Compositae**

The antiangiogenic effects of plant extracts and polyacetylenes isolated from *Bidens pilosa Linn.* was investigated[9]. Anti-cell proliferation, anti-tube formation, and cell migration assays were used for the valuation of bioactivities of target plant extracts and phytocompounds against angiogenesis. The result showed that an ethyl acetate fraction of *B. pilosa* exhibited significant anti-cell proliferation and anti-tube formation activities against human umbilical vein endothelium cells (HUVEC). This was the first report to demonstrate that polyacetylenes possess significant anti-angiogenic activities[9].

**Boerhaavia diffusa (Punarnava) family: Nyctaginaceae**

The extracts of *B. diffusa* reduced neovascularization. Acetone extracts showed highest inhibitory activity in angiogenic response; followed by benzene and alcohol extracts[10]. It seems to be consequences of interference of extracts in a) signaling of angiogenic agents from epithelial cells or b) cellular apoptosis, which in its absence results in normal CAM angiogenesis. These observations showed anti-angiogenic ethnomedical properties of this plant[10].

**Bombax ceiba (Silk cotton tree) family: Malvaceae (Bombacaceae)**

A methanol extract of the stem barks of *Bombax ceiba* was found to exhibit a significant anti-angiogenic activity on in vitro tube formation of human umbilical venous endothelial cells (HUVEC). Bioactivity-guided fractionation and isolation carried out on this extract afforded lupeol as an active principle. Lupeol showed a marked inhibitory activity on HUVEC tube formation while it did not affect the growth of tumor cell lines such as SK-MEL-2, A549, and B16-F10 melanoma[11].

**Camellia sinensis (Green tea catechin) family: Theaceae**

Epigallocatechin gallate (EGCG) from green tea has powerful anti-angiogenic properties[12]. Angiogenic factors in lesions and abdominal muscle were detected. EGCG, endometriotic lesions were smaller than control and glandular epithelium was smaller and eccentrically distributed. Angiogenesis in lesions from the implant and adjacent tissues was under-developed, and microvessel size and density were lower than control. EGCG significantly inhibited the development of experimental endometriosis through anti-angiogenic effects[12].

**Clerodendrum serratum (spreng.) (Timba task) family: Verbenaceae**

The methanolic extract of *C. serratum* (ME-CS) showed the most potent anti-angiogenic activity[13]. In another hand, qualitative study proved that ME-CS contains polyphenolics (hydrolysable tannins and flavonoids), terpenoids, saponins and may not contain any alkaloids. Therefore, while polyphenolics are the predominant compounds found in ME-CS, it is highly probable that they may play an important role in anti-angiogenic activity. Polyphenolics are responsible for anti-angiogenic effect of plants as herbal therapy such as *C. serratum* leaves[13].

Review

### Coffea arabica (Coffee) family: Rubiaceae

The effects of kahweol, an antioxidant diterpene contained in unfiltered coffee, on angiogenesis molecules. Kahweol showed an anti-angiogenic potential with inhibitory effects in two in vivo and one ex vivo angiogenesis models, with effects on specific steps of the angiogenic process: endothelial cell proliferation, migration, invasion and tube formation on Matrigel. Kahweol behaves as an anti-angiogenic compound with potential use in antitumoral therapies[14].

### Gardenia jasminoides (Gardenia) family: Rubiaceae

The EtOH extract of gardenia (*Gardenia jasminoides Ellis*) fruits was found to possess potent anti-angiogenic activity in the chick embryo chorioallantoic membrane (CAM) assay. Bioassay-guided fractionation and purification of the EtOH extract yielded an active anti-angiogenic compound, which was determined to be an iridoid glucoside, geniposide, by spectral analyses. Geniposide showed anti-angiogenic activity in a dose-dependent manner[15].

### Glycyrrhiza glabra (Licorice) family: Fabaceae

The effect of isoliquiritigenin (ISL) on angiogenesis development was investigated using ex ovo chick chorioallantoic membrane model[16]. Its effect on pathological angiogenesis was examined. Ex ovo chick chorioallantoic membrane assay showed that ISL dose-dependently suppressed VEGF-induced vessel growth. In vivo experiments illustrated that intravitreal ISL reduced vessel leakage. ISL was found to dose-dependently suppress VEGF and induce pigment epithelium derived factor expression in cultured endothelial cells. Using various experimental models of ocular neovascularisation, the authors[16] have demonstrated that ISL from licorice extract has an anti-angiogenic effect. The authors' findings suggest that ISL may be a potential anti-angiogenic molecule in the development of therapy for neovascularisation diseases[16].

### Parkia speciosa (Bitter bean) family: Fabaceae

The anti-angiogenic effect of eight extracts from *P. speciosa* empty pods was investigated[17]. In rat aortic rings, *P. speciosa* extracts significantly inhibited the microvessel outgrowth from aortic tissue explants by more than 50%. The anti-angiogenic activity was further confirmed by tube formation on matrigel matrix involving human endothelial cells[17].

### Salvia officinalis (Sage) family: Lamiaceae

The anti-angiogenic activity of *Salvia officinalis* extract was investigated[18]. *S. officinalis* aerial parts were extracted with ethanol and its successive hexane, ethyl acetate, n-butanol and aqueous fractions were evaluated for their anti-angiogenic activities using human umbilical vein endothelial cells (HUVEC) capillary tube formation and rat aorta models in a three-dimensional collagen matrix. The ethanol extract of *S. officinalis* (ESO) potently inhibited capillary tube formation in HUVEC and rat aorta models of angiogenesis, and its hexane fraction (HSO) exerted the highest inhibitory effect. These findings[18] indicated some new pharmacological activities of *S. officinalis* such as anti-angiogenic in vitro and ex vivo. Therefore, *S. officinalis* could be a candidate as a useful herb with therapeutic or preventive activity against angiogenesis related disorders[18].

### Silybum marianum (Milk thistle) family: Asteraceae

The anti-angiogenic effect of silymarin (SM) and its major pure component silibinin (SB), and also thalidomide (TH) was evaluated[19]. All 3 drugs showed concentration dependent inhibition of migration and differentiation assay. In an analysis of vascular endothelial growth factor secreted by LoVo cells, SM/SB/TH decreased. SM/SB has a strong anti-angiogenesis effect on the colon cancer cell line, and this might provide an alternative treatment option for anticancer treatment[19].

### Tillandsia recurvata L. (Jamaica ball moss) family: Bromeliaceae

The anti-angiogenic properties of a chloroform extract from the Jamaican ball moss was investigated using a modified version of the ex vivo aortic ring sprouting assay[20]. Angiogenesis was reduced in the presence of the chloroform crude extract when compared to the control. The results showed the promising anti-cancer properties of the Jamaican ball moss and may prove useful in anti-cancer agents' drug discovery[20].

**Withania somnifera (Ashwagandha) family: Solanaceae**

An anti-angiogenic potential of *Withania somnifera* was investigated by a chick chorio-allantoic membrane (CAM) wherein a significant inhibition of vascular endothelium growth factor (VEGF), induced neovascularization was recorded[21]. The effect was confirmed in vivo by mouse sponge implantation method. These findings[21] suggest that the roots of *Withania somnifera* possess anti-angiogenic activity, which may be a critical mediator for its anti-cancer action[21].

This review acts as a ready reference for anti-angiogenic properties of some plants to the scientific community, in specific to researchers and students looking for sources of knowledge of medicinal plants and leads for new bioactive compounds. It is to be kept in mind that the reported property may be shown by either the whole plant, or a part of the plant, or a particular extract, or isolated compounds. To know further about a biological action of a plant, it is advised to refer the individual research article. We hope the article will be of immense use to the researchers and students, and result in increased interest in these medicinal plants.

## REFERENCES


**[1]** J.Folkman; Nature.Med., **1**, 27-31 **(1995)**.
**[2]** W.Risau; Nature., **386**, 671-674 **(1997)**.
**[3]** J.Folkman, Y.Shing; J.Biol.Chem., **267**, 10931-10934 **(1992)**.
**[4]** N.Ferrara, T.Davis-Smyth; Endocr Rev., **18**, 4-25 **(1997)**.
**[5]** A.S.Mousa, S.A.Mousa; Nutr Cancer., **53(1)**, 104-10 **(2005)**.
**[6]** C.Cardenas, A.R.Quesada, M.A.Medina; Cell.Mol.Life.Sci., **63(24)**, 3083-9 **(2006)**.
**[7]** M.Sheela, Lingaraju, Kaveri Keshavaiah, P.Bharathi, Salimath; Drug Discov Ther., **2(4)**, 234-244 **(2008)**.
**[8]** A.Herrera Annabelle, C.Amor Evangeline; Journal of Medicinal Plants Research., **5(13)**, 2637-2646 **(2011)**.
**[9]** L.W.Wu, Y.M.Chiang, H.C.Chuang, S.Y.Wang, G.W.Yang, Y.H.Chen, L.Y.Lai, L.F.Shyur; Pharm Res., **21(11)**, 2112-9 **(2004)**.
**[10]** Jaywant Jadhav, Anuya Mane, Aruna Kanase; Int. J. Drug Dev. & Res., **3(4)**, 307-317 **(2011)**.
**[11]** Young-Jae You., Nguyen-Hai Nam., Yong Kim., Ki-Hwan Bae., Byung-Zun Ahn; Phytotherapy Research., **17(4)**, 341-44 **(2003)**.
**[12]** H.Xu., W.T.Lui., C.Y.Chu., P.S.Ng., C.C.Wang., M.S.Rogers; Hum.Reprod., **24(3)**, 608-618 **(2009)**.
**[13]** Ali Jimale Mohamed, Elsnoussi Ali Hussin Mohamed, Abdalrahim F.A.Aisha, Omar Ziad Ameer, Zhari Ismail, Norhayati Ismail, Amin Malik Shah Abdulmajid, Mohd Zaini Asmawi, Mun Fei Yam; Journal of Medicinal Plants Research., **6(3)**, 348-360 **(2012)**.
**[14]** C.Cardenas, A.R.Quesada, M.A.Medina; PLOS One., **6(8)**, e23407 **(2011)**.
**[15]** H.J.Koo, S.Lee, K.H.Shin, B.C.Kim, C.J.Lim, E.H.Park; Planta Med., **70(5)**, 467-9 **(2004)**.
**[16]** V.Jhanji, H.Liu, K.Law, V.Y.Lee, S.F.Huang, C.P.Pang, G.H.Yam; Br J.Ophthalmol., **95(9)**, 1309-15 **(2011)**.
**[17]** F.A.A.Aisha, K.M.Abu-Salah, S.A.Alrokayan, Z.Ismail, A.M.S.Abdul Majid; Pak J.Pharm.Sci., **25(1)**, 7-14 **(2012)**.
**[18]** M.Keshavarz, A.Mostafaie, K.Mansouri, A.Bidmeshkipour, H.R.Motlagh, S.Parvaneh; Phytother Res., **24(10)**, 1526-31 **(2010)**.
**[19]** Shung-Haur Yang, Jen-Kou Lin, Wei-Shone Chen, Jen-Hwey Chiu; Journal of Surgical Research., **113**, 133–138 **(2003)**.
**[20]** I.C.Henry Lowe, T.Charah Watson, Simone Badal, N.Eugene Ateh, J.Ngeh Toyang, Joseph Bryant; International Research Journal of Biological Sciences., **1(4)**, 73-76 **(2012)**.
**[21]** R.Mathur, S.K.Gupta, N.Singh, S.Mathur, V.Kochupillai, T.Velpandian; J.Ethnopharmacol., **105(3)**, 336-41 **(2006)**.