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Piper longum inhibits VEGF and proinflammatory cytokines and tumor-induced angiogenesis in C57BL/6 mice

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Abstract

The antiangiogenic activity of *Piper longum* was studied using in vivo as well as in vitro models. In vivo, antiangiogenic activity was studied using B16F-10 melanoma cell-induced capillary formation in C57BL/6 mice. Intraperitoneal administration of the extract (10 mg/dose/animal) significantly inhibited (50.6%) the number of tumor-directed capillaries induced by injecting B16F-10 melanoma cells on the ventral side of C57BL/6 mice. The cytokine profile in the serum of these animals showed a drastically increased level of proinflammatory cytokines such as IL-1β, IL-6, TNF-α, GM-CSF and the direct endothelial cell proliferating agent, VEGF. Administration of the methanolic extract of *P. longum* could differentially regulate the level of these cytokines. The level of IL-2 and tissue inhibitor of metalloprotease-1 (TIMP-1) was increased significantly when the angiogenesis-induced animals were treated with the extract. The extract of *P. longum* at non-toxic concentrations (10 μg/ml, 5 μg/ml, 1 μg/ml) inhibited the VEGF-induced vessel sprouting in rat aortic ring assay. Moreover, *P. longum* was able to inhibit the VEGF-induced proliferation, cell migration and capillary-like tube formation of primary cultured human endothelial cells. Hence, the observed antiangiogenic activity of the

plant *P. longum* is related to the regulation of these cytokines and growth factors in angiogenesis-induced animals.

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Keywords

Angiogenesis; Cytokine profile; *Piper longum*; Tube formation

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> ...Multiple studies have recommended the inhibitory action of natural product and dietary compounds on tumor specific angiogenesis (Dai et al., 2017; Huang et al., 2015; Ye et al., 2015). The study conducted by Sunil and Kuttan, suggest that the anti-angiogenic action of P. longum is associated to the regulation of proinflammatory cytokines growth factors in angiogenesis induced mice, along with inhibitory action on proliferation, migration and differentiation of endothelial cells (Sunila and Kuttan, 2006). Thus, it can be concluded that P. longum has novel molecular mechanism that restrict the mutual angiogenic signaling pathways, however, the animal experiments did not establish dose-effect relationship....

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Review on potential antiviral and immunomodulatory properties of Piper Longum

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Abstract

Piper longum traditionally known as Pippali is a climbing vine belonging to the Piperaceae family, which originated in northeastern India and the Western Ghats. It is majorly used in traditional and Ayurvedic system of medicines to treat bronchitis, diarrhea, viral hepatitis, respiratory infections, stomach pain, bronchitis, spleen diseases, coughs, colds and tumors. Articles indexed by Scopus, electronic search as Science Direct, PubMed, are used to collect information about Piper longum. There are many phytochemicals in Pippali, including alkaloids, essential oils, flavonoids and steroids. The pharmacological properties reveal the anti-inflammatory, anti-

microbial, adulticidal, anti-obesity, anti-fungal, antipyretic and cardio protective effects of the plant. Pipili also has many antiviral activities, and helps to improve the immune system and effectively resist hepatitis B virus. This plant seems to be non-toxic, easy to obtain, inexpensive, and has no side effects. Although there are infinite traces for its medicinal use, however its use in treating viral influenza like diseases is not yet much explored. However, it has strong potential to treat symptoms such as cough, cold and fever. In the wake of the current situation of the global corona virus, it has become essential to look for alternatives that would be effective against the virus as well as provide the additional immunity boosting ability. Therefore, effective experimentation and investigations are essential to consider its competence. Researchers must study the plan