

## **What is Honokiol Extract (Magnolia Tree)**

Medicinal plants are known to be the source of many common pharmaceuticals. Drugs derived from the plant kingdom include aspirin from white willow, digitalis from foxglove, morphine from poppy, and **chemotherapy** agents like vincristine from periwinkle and taxol from the yew. Many herbs and plants also play a supportive role in conjunction with conventional cancer therapy. One such natural compound is **honokiol**, extracted from the magnolia tree. Traditionally used in Japanese and Chinese herbal medicines, honokiol has been found to be a powerful, versatile tool in integrative cancer treatment.

A highly active compound derived from magnolia bark, honokiol has been used in Traditional Chinese Medicine (TCM) for treating digestive disorders, anxiety and other chronic conditions. Over the last decade or so, honokiol has been the subject of extensive research as an adjuvant cancer treatment, demonstrating remarkable benefits through diverse mechanisms of action. The compound shows promise for a number of solid tumors and hematological cancers and appears to be particularly effective in reversing multi-drug resistance and synergizing with other treatments.

### **Mechanisms of Action**

A growing body of data demonstrates honokiol's multiple mechanisms of action against **cancer**. Honokiol appears to be particularly active in regulating cell cycle arrest and promoting apoptosis (programmed cancer cell death) by inhibiting a number of cancer signaling pathways.

A July 14, 2008 article in ***Science Daily*** reported on research from Emory University in Atlanta showing that this natural magnolia compound interferes with a critical pathway for cancer growth that was previously considered "undruggable." Specifically, it blocks survival signals from a difficult-to-target family of genes in **breast**, **lung** and **bladder** cancer cells.<sup>1</sup>

A comprehensive 2011 review highlights the multiple pathways by which honokiol influences apoptosis and inhibits multiple cancer cell types including **breast**, **prostate**, **colon**, **liver**, **lung** and others.<sup>2</sup> In non-small cell lung cancer, honokiol inhibited cancer growth and induced apoptosis.<sup>3</sup> In **leukemia**, honokiol promoted cell cycle arrest and apoptosis by blocking cancer survival signals.<sup>4</sup> A 2012 study showed honokiol halted growth and metastasis of **melanoma**.<sup>5</sup> Another study demonstrated that honokiol-induced cell cycle arrest irrespective of the hormone sensitivity of **prostate cancer** cells.<sup>6</sup>

Honokiol can also inhibit tumor angiogenesis by modulating various signaling pathways that promote cancer cell growth. Honokiol has been shown to inhibit the spread of cancer cells through the lymph system by inhibiting one of the primary pathways involved in growth stimulation related to VEGF (vascular endothelial growth factor).<sup>7</sup> A

2012 study showed that honokiol inhibited angiogenic pathways to slow the spread of **gastric cancer**.<sup>8</sup>

Another 2012 study showed honokiol's direct cytotoxic activity, showing the compound attacked **metastatic bone cancer** cells directly.<sup>9</sup> Honokiol is highly bioavailable and its small molecular size allows it to reach target tissues and cross the blood-brain and blood-cerebrospinal fluid barriers, making it an excellent adjunct for **brain tumors** like gliomas and neuroblastomas.<sup>10, 11</sup>

## **Synergistic with Cancer Treatments**

One of honokiol's most important attributes is its ability to act synergistically with conventional cancer treatments. Numerous studies show the remarkable ability of honokiol to enhance the effectiveness of radiation and certain chemotherapy drugs in a number of cancers, including the following studies conducted between 2005 and 2013 which demonstrated that honokiol:

- Synergized with chemotherapy drugs in multidrug resistant **breast cancer**<sup>12</sup>
- Sensitized treatment-resistant colon cancer cells to radiation therapy<sup>13</sup>
- Enhanced the action of cisplatin against **colon cancer**<sup>14</sup>
- Re-sensitized cancer cells to doxorubicin in multidrug resistant uterine cancer<sup>15</sup>
- Performed synergistically with the drug imatinib against human leukemia cells<sup>16</sup>
- Sensitized cancer cells to radiation treatments<sup>17</sup>
- Potentiated the activity of cisplatin in animal models of ovarian cancer<sup>18</sup>
- Enhanced the cytotoxicity of drugs used for B-cell chronic lymphocytic leukemia<sup>19</sup>

## **Anti-inflammatory and Antioxidant Protection**

In addition to its direct anticancer actions, honokiol is also shown to offer other valuable anti-inflammatory and anti-oxidative effects that relate to its mechanisms against cancer. Honokiol offers powerful free radical scavenging benefits against reactive oxygen species.<sup>20,21</sup> Its inhibition of reactive oxygen was actually shown to be 1,000 times that of  $\alpha$ -tocopherol (vitamin E).<sup>22</sup> (Interestingly, honokiol is also a selective pro-oxidant, generating reactive oxygen against certain cancer cells. The ability of honokiol to function either as an antioxidant or a pro-oxidant depending on the need is one of its most remarkable features.) A 2005 study suggested honokiol can protect the brain against amyloid plaque neurotoxicity in the formation of Alzheimer's disease<sup>23</sup> by reducing inflammation and oxidation in the brain.

## **Source and Dosages**

The most concentrated and purest source of honokiol is [HonoPure](#) by EcoNugenics, offering 98% pure honokiol extract for multiple indications. The company has agreed to offer BeatCancer.org clients a 15% discount on honokiol, as well as their entire line of products for prostate health, breast health, immune support, hormonal support, and heavy metal detoxification, among others.

Below are suggested dosages according to clinical use guidelines:

- Active cancer: 1 g x 3/day (starting at lower dosage and building up to full dose)
- Cancer prevention/post cancer therapy: 1 g/day
- Inflammatory conditions: 250-500mg x 2/day
- Anxiety: 250 mg x 2/day

Honokiol's *in vivo* toxicity record thus far shows it to be extremely safe.

## Conclusion

The research on this remarkable compound continues to show beneficial effects for numerous serious and difficult-to-treat conditions, including protection against neurological conditions like Alzheimer's disease<sup>23</sup> and stroke damage,<sup>24</sup> viral and bacterial infections like hepatitis C,<sup>25-26</sup> and multiple drug resistant cancer. It is currently used clinically by a growing number of integrative and naturopathic physicians. **SOURCE: Science Daily – Emory University – July 14, 2008**

### JOURNAL:

Xu HL, Tang W, Du GH, Kokudo N. Targeting apoptosis pathways in cancer with magnolol and honokiol, bioactive constituents of the bark of *Magnolia officinalis*. *Drug Discov Ther.* 2011 Oct;5(5):202-10. [3] Singh T, Prasad R, Katiyar SK. Inhibition of class 1 histone deacetylases in non-small cell lung cancer by honokiol leads to suppression of cancer cell growth and induction of cell death *in vitro* and *in vivo*. *Epigenetics.* 2013 Jan;8(1):54-65. [4] Ishikawa C, Arbiser JL, Mori N. Honokiol induces cell cycle arrest and apoptosis via inhibition of survival signals in adult T-cell leukemia. *Biochim Biophys Acta.* 2012 Jul;1820(7):879-87. [5] Kaushik G, Ramalingam S, Subramaniam D, Rangarajan P, Protti P, Rammamoorthy P, Anant S, Mammen JM. Honokiol induces cytotoxic and cytostatic effects in malignant melanoma cancer cells. *Am J Surg.* 2012