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The Therapeutic Effects of per os Artemisinin Delivered as Dried Leaf Artemisia annuavs. Artesunate in Non-small Cell Lung Cancer

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Et al.

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Artemisinin, the active component of *Artemisia annua* L. used to treat malaria, also has therapeutic efficacy against many types of cancer. Solubility issues led to development of more soluble semi-synthetic derivatives. Artesunate (ART), in particular, is a more soluble derivative of artemisinin and has profound cytotoxicity toward many types of tumor cells, but healthy cells are less sensitive. Artemisinin delivered *per os* as dried leaves, referred to as dried leaf artemisinin (DLA), was shown in rodent studies to improve bioavailability by more than 40-fold. ART has been widely studied for its anti-cancer properties, but it has yet to be shown if DLA also improves therapeutic efficacy. As *A. annua* produces a wide array of phytochemicals with anti-cancer activity other than artemisinin, it is reasonable to expect DLA may provide a more potent therapeutic. Using two non-small cell lung cancer cell lines, PC-9 and H1299, artemisinin delivered as DLA effectively reduced viability with 24h IC_{50} values of 56.3 and 77.5 µM for PC-9 and H1299, respectively, as determined by MTT assay. For PC-9 cells, this was a 2.5-fold improvement in the 24h IC_{50} value for ART at 142.9 µM. However, for the H1299 cells, ART at 60.6 µM was better than DLA by about 25%. Ongoing studies are comparing the mechanism of action of DLA and ART on these two cell lines and will analyze markers for apoptosis, proliferation and metastatic migration and invasion. Xenograft models also will be used to compare *in vivo* efficacy of DLA and ART on tumor reduction. These studies will help us further understand the anti-cancer effects of artemisinin when delivered *per os* as dried plant leaves.

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