Summary of the Weathers lab research into use of Artemisia annua as a therapeutic

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Our overall goal is to use science to explain how Artemisia annua, and sometimes A. afra, work as a highly bioavailable therapeutic for treating malaria, schistosomiasis and tuberculosis (initiated in 2018).

Below lists our efforts related to this goal:

- Artemisinin delivered via orally consumed dried leaf A. annua (DLA) in animal models was ~45 fold more bioavailable than when delivered as a pure compound (Weathers et al. 2011 Weathers et al. 2014a).
- Artemisinin from DLA (aka pACT) persisted longer in diseased mice than in healthy ones per a 2 hr pharmacokinetic study (Weathers et al. 2014a).
- Artemisinin delivered as DLA in an animal model was five times more active in killing malaria parasites (Elfawal et al. 2012).
- DLA was more effective than artemisinin in treating artemisinin-resistant malaria in rodents. (Elfawal et al 2015).
- DLA was at least three times more resilient against emergence of artemisinin drug resistance than the pure drug. (Elfawal et al. 2015).
- We made and analyzed DLA tablets (Weathers and Towler 2014).
- We tracked the stability of artemisinin, total flavonoids, and monoterpenes in stored DLA for >2 yrs and showed that only the latter declined with age (Gruessner et al. 2019).
- We tested efficacy on digestive release of DLA phytochemicals from different capsules (Weathers et al. 2014b); Capsugel Plant caps and Vcaps Plus allowed excellent release of artemisinin from the plant material (Desrosiers and Weathers 2016; Desrosiers et al. 2019).
- Using Caco2 cells, we also showed that essential oils helped improve the transport of artemisinin across the intestinal wall (Desrosiers and Weathers 2018; Desrosiers et al. 2019).
- We showed that artemisinin is stable in a liter of tea infusion stored at room temperature for 24 hr, but flavonoid content declines. (Weathers and Towler 2012)
- As part of an international team we showed that DLA tablets effectively treated >100 patients with severe malaria who did not respond to either artesunate-lumefantrine (AL) or iv artesunate (Daddy et al. 2017).
- As part of a large international team, we showed that DLA tea infusion was equally effective as praziquantel (PZQ) in treating schistosomiasis in human patients and that DLA had far fewer adverse side effects than PZQ (Munyangi et al. 2018).

- As part of a large international team, we showed that DLA tea infusion was far more effective than a standard artemisinin combination therapy (ASAQ) in treating malaria in human patients and that DLA had far fewer adverse side effects than ASAQ (Munyangi et al. 2019).
- As part of a large international team, we showed that DLA tea infusion was far more effective than a standard artemisinin combination therapy (ASAQ) in eliminating malaria gametocytes in human patients (Munyangi et al. 2019).
- Using in vitro cultures of P. falciparum we have showed that A. annua DLA tea infusions inhibit both early and late genes that control gametocyte development thereby breaking the cycle of malaria (Snider and Weathers, manuscript in preparation).
- We showed that the essential oils in DLA enhance solubility of artemisinin thereby improving its bioavailability when delivered as DLA (Desrosiers and Weathers
- In rats, we have absorption, distribution, metabolism, excretion (ADME) data showing significantly more DLA-delivered artemisinin is provided to a broad range of organs than from artemisinin (Desrosiers et al., manuscript in preparation).
- In rats, we also showed greater reduction of inflammation markers TNF-α and IL6 from DLA than from artemisinin (Desrosiers et al., manuscript in preparation).
- In rats, we showed that DLA-delivered artemisinin ADME and inflammation responses were greater in females than in males (Desrosiers et al., manuscript in preparation).
- Using liver microsomes, we showed that DLA substantially improves artemisinin bioavailability by inhibiting the cytochrome P450s that metabolize artemisinin and its derivatives, CYP3A4 and CYP2B6 (Desrosiers et al., manuscript in preparation).
- We developed a high artemisinin and flavonoid cultivar of A. annua that we have shown is best harvested at its preflowering stage and maintains a consistent phytochemical content if propagated via rooted cuttings over years of field cultivation (Towler and Weathers 2015; Gruessner et al. 2019).
- Based on our agricultural field trials and the ICIPE (2005) study we estimated that use of therapeutic DLA is highly economical at $0.10-0.35/cure (Weathers et al. 2014c).
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