enhance the effectiveness of these plant-based medicines in angiotherapy (5). Dantonic® is an oral formulation for the treatment of angina, currently undergoing global Phase **III** clinical trial. It consists of extracts from dried roots of *Salvia miltiorrhiza* (Danshen) and *Panax notoginseng* (Sanqi), plus borneol. Previously, a novel phenolic ester isopropyl 3- (3, 4-dihydroxyphenyl)-2 -hydroxypropanoate (IDHP) derived from danshensu was found to be a major metabolite of Dantonic® in human plasma and rabbit hearts (6). It produced a concentration-dependent (0.0001–30 μM) relaxation of norepinephrine-induced contraction in endothelium-intact and endothelium-free mesenteric arterial rings, mainly by causing the relaxation of smooth muscles through its actions on calcium-activated potassium channels (7). We hypothesise that chimeric esters of S. *miltiorrhiza* phenolic acids and borneol may improve the pharmacodynamic and pharmacokinetic profiles of the parent phenolic acids. To test their potential in therapeutic angiogenesis, IDHP and six chimeric esters were tested on human umbilical vein endothelial cells (HUVECs) for their ability to modulate migration, proliferation and tube formation *in vitro.* Some chimeric esters (1.0 nM-10 μM) stimulated HUVEC proliferation and migration, but had no significant effect on tube formation. Preliminary studies indicate that these chimerics stimulate HUVECs by inhibiting p38 mitogen-activated protein kinase. IDHP did not affect HUVEC proliferation but was cytotoxic at >50 μM, and its effect on HUVEC migration and tube formation are currently under investigation. Overall, this series of studies highlights a new platform for drug discovery based on the holistic principle of traditional Chinese medicine and synergistic interactions between materia medica, and introduces several novel drug candidates for angiogenesis modulation.

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IDENTIFICATION OF THASPINE AS NOVEL TOPOISOMERASE INHIBITOR, IN A SPHEROIDS BASED SCREENING

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Aim of work — identification of effective compound (s) against solid tumors. The NCI Natural Products Set (221 compounds) was screened for apoptosis induction on HCT116 colon carcinoma human tumor cell line. The cell line was grown three dimensionally as spheroids in the 96-well plate. Apoptosis was detected using M30-CytoDeath ELISA assay. A preliminary indication for the mechanism of action of identified hits was determined through CMAP experiments, which was confirmed by a specific in vitro assay. SCID mice injected with HCT116 and FaDu cell lines were used for in vivo evaluation of identified hits. The screen led to the identification of thaspine, an alkaloid from the South American tree *Croton lechleri*, as a proapoptotic compound in HCT116 spheroids. Analysis of the gene expression signature of thaspine-treated cells, using the connectivity map (CMAP) technique, suggested that thaspine is a topoisomerase inhibitor. Thaspine inhibited both topoisomerase I and II enzymes in vitro. Finally, the compound induced apoptosis in two xenograft mouse models (FaDu & HCT116), and significant, though transient, tumor size reduction in FaDu model. Statistical significance was calculated using Student's t-test. The alkaloid thaspine, is a novel dual topoisomerase inhibitor, effective on human colon carcinoma spheroids with significant anticancer activity in vivo.