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Privileged Structure: Novel Indane Scaffolds as Potential Anticancer and Anti-Inflammatory Agents

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The identification and use of “privileged structures” can increase the reliability and shorten the process in the drug discovery and drug design (a-b). Indane scaffolds occur in various natural products and they constitute the privileged structure that is ubiquitous in many biologically and pharmaceutically active molecules (c-e). Our research group has been working on the synthesis and pharmacological activity of nature identical and synthetically modified indanes and indanones for 20 years. In the current study, the molecular design is centred on elaboration of a fern derived bioactive pharmacophore. The fern is used in traditional Taiwanese medicine to treat inflammation, allergy, stomach cramps and fever (f). Using a synthetic approach we have designed a novel chemical scaffold which can be modified to inhibit angiogenesis and 5-lipoxygenase activity. The parent scaffold and a number of strategically modified derivatives were initially screened using the Zebra fish (*Danio rerio*) model of tumour angiogenesis (g). This screen led to the identification of two lead molecules, which were then further evaluated in *in vitro* cell lines and colorectal explants. Results from these experiments establish that the lead compounds affect inter-segmental vessel formation. These molecules also inhibit cell invasion and tube formation. When evaluated in *ex vivo* colorectal cancer explants where the molecules significantly affected angiogenic and inflammatory protein secretions. These small molecules also alter gene expression. Modification of the scaffold can inhibit 5-lipoxygenase activity. These data suggest that the new scaffold may have significant potential in the treatment of angiogenesis and inflammatory related diseases.

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