Lepidotols and lepidotins: new phenylcoumarins from Mesua lepidota as promising inhibitors of endothelial immune responses and dysfunction

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Résumé en anglais	During organ transplantation, graft endothelium is the first barrier encountered by immune cells of the recipient. Endothelial cells surface presents inflammatory and immune proteins which are over-expressed after activation by pro-inflammatory cytokines, Damage Associated Molecular Patterns (DAMPs) or Advanced Glycation End Products (AGEs) [1]. Among natural products, several polyprenylated polyphenols have shown anti-inflammatory, immunomodulatory and anti-AGEs properties [2 – 3]. Such secondary metabolites are biosynthesized by Calophyllaceae species such as Calophyllum or Mesua species. In order to identify natural products able to prevent endothelial dysfunction, a dereplication analysis was conducted on various extracts from Calophyllum and Mesua species native to Malaysia. It appeared that the fruits of Mesua lepidota T. Anderson are a rich source of original phenylcoumarins named as lepidotols and lepidotins. The main compound, lepidotol A, was evaluated for its anti-inflammatory, immunomodulatory and anti-AGEs potential. Beside a potent inhibitory effect of the VCAM-1, class II HLA and HLA-E induced surface-expressions on human endothelial cells (52%, 97% and 66%, respectively), lepidotol A exhibited an inhibition of AGEs formation five to thirty times higher than aminoguanidine (positive control). These results are consistent with the marked pharmacological activities of prenylated aromatic metabolites [4], and highlight a new approach to discover protective compounds against graft rejection.
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