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Clusianone derivatives: Separation, semi-synthesis and anticancer evaluation against squamous carcinoma of the nasopharynx and lung adenocarcinoma

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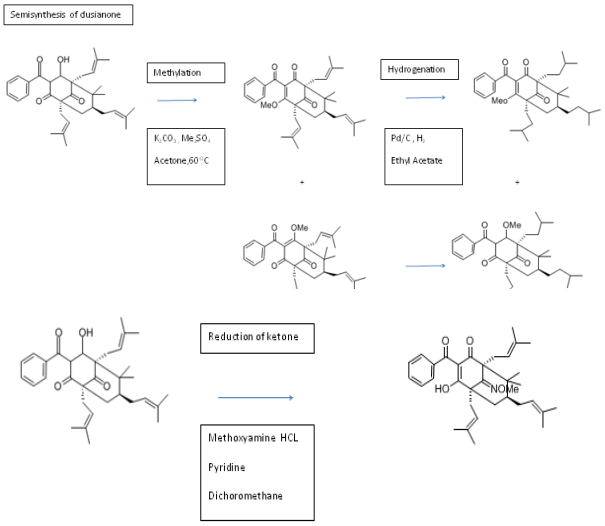
Natural clusianone belongs to compounds classified as type B polyprenylated polycyclic acylphloroglucines (PPAPs). PPAPs have a common central bicyclo[3.3.1]nonane-2,4,9-trione surrounded by four substituents at certain relative position and configuration. They are a family of natural product with wide range of compelling biological activities. A number of strategies have been explored to obtain clusianone through total synthesis to date. However there is no research done on clusianone derivatives via semi-synthetic methods. This approach is by semi-synthesis of clusianone isolated from *Garcinia sp*. We also developed an isolation method that optimizes clusianone extracts as crystalline solid. Some of the semi-synthesis methods employed is hydrogenation, methylation and ketone reduction via addition of amine derivatives. Further studies of the role of the clusianone derivatives are presented in its *in vitro* anticancer activity. The research includes the semi-synthetic approach, clusianone and its derivatives analogues, their mechanism of action and structure activity relationships. Taxotere is used as a reference known as the most successful anticancer drugs developed and utilized during the past two decades. The reference compound is used to identify which features are responsible for binding the receptor of interest and to rationally relate the structure activity relationship of which pharmacophores of clusianone should be target of semi synthesis to enhance the bioactivity as an anticancer drug. Conversely, the clusianone prenyl groups were hydrogenated using Pd catalayst to produce derivatives which possess hydrophilic regions. However, in order to circumvent side reactions on clusianone, it has to be methylated. In subsequent semi-synthesis approach is through ketone reduction via addition of amine derivatives where ketone group is less sterically hindered by benzoyl group in clusianone. We report here clusianone and derivatives compounds for anticancer activity against human mammalian cells with focus on human respiratory cells which includes NP69 Immortalized nasopharyngeal epithelial cell (normal cells), HK1 squamous carcinoma of the nasopharynx (carcinoma cells), MRC5 lung fibroblast (normal cells) and A549 lung adenocarcinoma (carcinoma cells).



Biography

Teng-Jin Khoo completed his Ph.D. under the supervision of Prof. Karen A. Crouse at University Putra Malaysia. In 2006, he joined School of Pharmacy, The University of Nottingham and currently is an Associate Professor teaching Medicinal Chemistry. His research focuses on the separation, semi-synthesis and structure-activity relationship of plant natural products with cholesterol lowering or anticancer properties. He is also widely in collaboration working on synthesis of dithiocarbazate based Schiff base ligands and its structure-activity relationship. He has published more than 15 papers in international reputable journals and works are cited over 180 times.

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