

学位論文審査結果の要旨

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<p>(学位論文審査結果の要旨)</p> <p>A novel orexin antagonist from a natural plant was discovered using zebrafish behavioural analysis</p> <p>【主論文審査結果の要旨】</p> <p>著者らは論文において下記の内容を述べている。</p> <p>OBJECTIVE: Phenotypic screening is one of the most practical approaches to the identification of mediators of behaviour, since it is difficult to model brain function <i>in vitro</i>, at a cellular level. We used a zebrafish (<i>Danio rerio</i>) behavioural assay to discover novel, natural, neuroactive compounds.</p> <p>MATERIALS AND METHODS: A zebrafish behavioural assay was performed for seven natural compounds, obtained from plants. The behavioural profiles were compared to those of known psychoactive drugs. We characterised a natural compound exhibiting a behaviour profile similar to that of suvorexant, using <i>in silico</i>, <i>in vitro</i> and microarray expression analysis.</p> <p>RESULTS: The behavioural analysis performed in this study classified central nervous system drugs according to their mechanism. Zebrafish treated with a natural compound, 8β-(4'-Hydroxytigloyloxy) costunolide (8β), showed behaviour profiles similar to those of zebrafish treated with suvorexant, a known orexin antagonist. This behavioural assay was validated using <i>in silico</i> and <i>in vitro</i> assays, which revealed that the new compound was a dual orexin receptor antagonist. In addition, transcriptome analysis suggested that 8β might regulate the nuclear factor-κB (NF-κB) related pathway.</p> <p>CONCLUSIONS: We conclude that zebrafish phenotypic screening, combined with <i>in silico</i> assays and gene expression profiling, is a useful strategy to discover and characterize novel therapeutic compounds, including natural products.</p> <p>本論文は、ゼブラフィッシュ行動解析法が天然機能性素材の表現型に基づく探索に有用であり、また、遺伝子発現解析と組み合わせて表現型に紐づいた作用メカニズム</p>			

の推測が可能であることを示した論文であり、学術上極めて有益であり、学位論文として価値あるものと認めた。

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