（様式３号）

学 位 論 文 の 要 旨

氏名 ZHANG MIN（張 敏）

〔題名〕

The different effects of acacetin and biochanin A on SPC-induced abnormal vascular smooth muscle contraction
（SPC誘発性血管平滑筋の異常収縮に対するアカセチンとビオカニン Aの異なる効果）

〔要旨〕

Unlike Ca^{2+}-dependent normal vascular contraction, the Rho-kinase-mediated Ca^{2+}-independent abnormal vascular contraction mediates cerebral and coronary vasospasm. As an upstream key molecule of such abnormal Ca^{2+}-independent vasocontraction, we identified sphingosylphosphorylcholine (SPC) and Fyn tyrosine kinase. The ideal therapeutic agent for vasospasm is to specifically inhibit Ca^{2+}-independent contraction without affecting Ca^{2+}-dependent one. We previously found the ideal drug eicosapentaenoic acid (EPA) and indeed EPA clinically suppressed human vasospasm after subarachnoid hemorrhage. However, lipophilic EPA can't be administered intravenously. Therefore, it's urgent to find a new water-soluble compound with the same effects as EPA.

We screened plant-derived compounds and focused on flavonoids, acacetin and its structural isomer biochanin A which is only different in the position of phenyl group in chemical structure. Acacetin slightly inhibited 40 mM K^+-induced Ca^{2+}-dependent contraction in porcine coronary vascular smooth muscle (VSM) strips, but inhibited the SPC-induced Ca^{2+}-independent contraction fast and strongly. In contrast, biochanin A inhibited 40 mM K^+-induced contraction more strongly than the SPC-induced contraction. Pre-incubation of acacetin and biochanin A showed inhibitory effect on SPC and 40 mM K^+-induced contractions indicating that they had a superior preventive effect on vascular contractions. The morphological changes induced by SPC in human coronary smooth muscle cells were also inhibited by acacetin and biochanin A. Both acacetin and biochanin A strongly inhibited SPC-induced Rho-kinase activation and myosin light chain phosphorylation.

In summary, the difference in the position of the phenyl group on acacetin and biochanin A is involved in the inhibitory effect on SPC-induced abnormal contraction.

（様式９号）

学位論文審査の結果の要旨

令和　３年　２月25日

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学位論文題目名（題目名が英文の場合、行を変えて和訳を括弧書きで記載する。）

The different effects of acacetin and biochanin A on SPC-induced abnormal vascular smooth muscle contraction

（SPC誘発性血管平滑筋の異常収縮に対するアカセチンとビオカニンＡの異なる効果）

学位論文の関連論文題目名（題目名が英文の場合、行を変えて和訳を括弧書きで記載する。）

血管平滑筋の異常収縮に対するアカセチンとビオカニンＡの異なる効果について

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In summary, the difference in the position of the phenyl group on acacetin and biochanin A is involved in the inhibitory effect on SPC-induced abnormal contraction.

本論文は、アカセチンとビオカニンＡとの構造比較を通してSPCによるCa^{2+}非依存性収縮に対する抑制作用を詳細に検討したものであり、学位論文として価値あるものと認めた。

備考　審査の要旨は８００字以内とすること。