

# アンピシリンによる腸内細菌叢の構成変化に関わらず rhein 8-O- $\beta$ -D-Glucopyranoside は 大黃甘草湯の下剤活性を維持させる

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*Biological & Pharmaceutical Bulletin*, 39, 378-383 (2016)

## Rhein 8-O- $\beta$ -D-Glucopyranoside Elicited the Purgative Action of Daiokanzoto (Da-Huang-Gan-Cao-Tang), Despite Dysbiosis by Ampicillin

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**ABSTRACT:** Sennoside A (SA), the main purgative constituent of Daiokanzoto (da-huang-gan-cao-tang: DKT), is generally regarded as a prodrug that is transformed into an active metabolite by  $\beta$ -glucosidase derived from *Bifidobacterium* spp. Therefore, DKT is to combine it with antibiotics promoting dysbiosis, thereby it is suggested the purgative activity of DKT inhibited. In this study, ampicillin was administered to mice for eight days, and it was investigated that changes in the SA metabolism of SA alone and DKT. The results showed that the SA metabolism of SA alone continued to be inhibited by ampicillin, but that of DKT was activated from day 3 under the same conditions. For the purpose of investigating the mechanism of SA metabolism activated of DKT in the mice administered ampicillin, changes in the SA metabolism were observed in the presence of rhein 8-O- $\beta$ -D-glucopyranoside (RG) in rhubarb and liquiritin in glycyrrhiza, both of which accelerated the SA metabolism. In fact, RG achieved an activation of SA metabolism similar to that by DKT. The purgative action of DKT, which was continued treatment of the ampicillin, was significantly greater than that by SA alone, and it was shown that RG was involved in this effect. Furthermore, we analyzed changes in intestinal microbiota before and after administration of ampicillin. No Bifidobacteria were detected throughout the treatment, but Bacteroides were significantly increased after days 3 under the same conditions. Taken together, these results strongly suggested that the RG in DKT changed the function of Bacteroides and thereby allowed DKT to metabolize SA.

**抄録** 大黃甘草湯 (DKT) の主有効成分であるセンノシド A (SA) は、ビフィズス菌が有する  $\beta$ -グルコシダーゼによって代謝変換され下剤活性を示す。そのため、腸内細菌叢の構成を変化させる抗菌薬の併用により、DKT の下剤活性は抑制されることが示唆される。本研究では、アンピシリンを 8 日間経口投与して、SA 単独および DKT について SA 代謝変化を検討した。その結果、アンピシリンによって SA 単独の SA 代謝

は抑制され続けたが、DKTのSA代謝はアンピシリン投与3日日以降から賦活した。そこで、DKTによるSA代謝賦活作用について、SA代謝促進作用を有する大黄に含まれる rhein 8-*O*- $\beta$ -D-glucopyranoside (RG) および甘草に含まれるリクイリチンについてその影響を検討した結果、RGはDKTと同様にSA代謝賦活作用を示した。下剤活性評価においても、SA単独と比較してDKTの下剤活性は有意に促進し、その作用にRGの関与が認められた。さらに、アンピシリン投与前後の腸内細菌叢を解析したところ、アンピシリン投与によってビフィズス菌は全く検出されなかったが、アンピシリン投与3日日以降からバクテロイデスは有意に増加した。以上の結果から、RGはバクテロイデスの機能を変化させてSA代謝能を与えることによりDKTの下剤活性を賦活したことが強く示唆された。