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論　文　内　容　の　要　旨
Synopsis of Thesis

氏　　名 Name	YE XIN
論文題名 Title	Effect of Si-based agent on alcohol hangovers and liver damage caused by acute ethanol overdose （急性エタノール過量投与による二日酔いおよび肝障害に対するシリコン製剤の影響）

論文内容の要旨

〔目　的(Objective)〕

This study aimed to evaluate whether a silicon (Si)-based agent, which continuously generates hydrogen in the intestine, can alleviate alcohol-induced motor impairment and mitigate ethanol (EtOH)-induced liver injury in an acute EtOH-overdose mouse model.

〔方法ならびに成績(Methods/Results)〕

Male C57BL/6J mice were assigned to either a control diet or a diet containing 2.5% Si-based agent for one week before intraperitoneal administration of distilled water or 30% EtOH (3.8 mg/g body weight). Four groups were compared: Con, Si, Con-EtOH, and Si-EtOH. Behavioral assessments were performed 20 hours after EtOH administration and included measurements of spontaneous activity (Supermex system), open-field testing (distance, speed, activity time), and rotarod testing to assess motor coordination. Liver injury was evaluated by hematoxylin–eosin (HE) staining of paraffin-embedded liver sections and quantified by the percentage of damaged area and hemorrhagic area across multiple fields. Serum assays measured oxidative stress (d-ROMs, BAP), blood acetaldehyde, and activities of EtOH-metabolizing enzymes (ALDH, catalase).

Compared with the Con-EtOH group, the Si-EtOH group exhibited significantly attenuated reductions in spontaneous activity and open-field locomotion (distance, speed, and activity time), and significantly improved rotarod retention time, indicating mitigation of EtOH-induced motor dysfunction. HE stain showed that the Con-EtOH group presented widespread hepatocellular vacuolation and localized hemorrhage around interlobular veins, whereas the Si-EtOH group displayed markedly fewer vacuolated hepatocytes and reduced hemorrhagic areas; quantification confirmed a significant reduction in the percentage of damaged liver tissue in the Si-EtOH group. In serum analyses, blood acetaldehyde concentrations did not differ significantly among groups at the 20-hour time point. Notably, ALDH activity remained elevated in the Con-EtOH group, but was not elevated in the Si-EtOH group, suggesting an earlier completion of EtOH metabolism or a faster return to baseline in the latter. Antioxidant capacity (BAP) tended to increase in the Si-EtOH group compared with the Si group, although this change did not reach statistical significance.

〔総　括(Conclusion)〕

Administration of the Si-based agent mitigates alcohol-induced motor impairment and reduces EtOH-associated liver damage in an acute overdose mouse model. The protective effects are associated with a histologically demonstrable reduction of hepatic vacuolation and hemorrhage (on HE), a tendency toward enhanced systemic antioxidant capacity in the Si-EtOH group, and differences in the temporal profile of ALDH activity between Si and Si-EtOH groups. These results support the potential of the Si-based agent as a therapeutic strategy to alleviate alcohol-related hangover symptoms and attenuate alcohol-induced liver injury.

論文審査の結果の要旨及び担当者

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論文審査の結果の要旨

本研究では、腸内で水と反応して水素を持続的に産生するシリコン製剤が、急性の大量飲酒による二日酔い症状や肝障害を軽減できるかを、マウスモデルを用いて検討した。行動解析では、投与20時間後に自発運動量や運動機能に大きな変化は見られなかったが、新しい環境での探索行動の低下は本製剤により有意に改善した。肝組織の観察では、対照群で脂肪の蓄積や出血を伴う肝障害が認められたのに対し、本製剤投与群ではこれらの障害が軽減していた。血清解析では多くの指標が20時間後に回復していたが、アルコール代謝に関与するALDH活性には群間で異なる傾向が見られ、代謝の進み方に違いがある可能性を示した。以上より本製剤は二日酔いおよび急性アルコール中毒に対する新たな治療候補となり得る。これらの論文内容について審査した結果、本論文は博士（医学）の学位授与に値する。