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Analysis of Therapeutic Effects of Paeonol on *Candida albicans* Aggravated Alcoholic Liver Disease (ALD) through Dectin-1/TLR2/NLRP3 Pathway

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SUMMARY. **Alcoholic liver disease (ALD) is caused by long-term alcohol consumption and is associated with the changes in the composition of intestinal mycobiota, especially *Candida albicans*. Pharmacological therapy to improve intestinal ecological imbalance is becoming a promising strategy for ALD treatment. An ALD model induced by *C. albicans* was established in C57BL/6 mice using a well-defined chronic-plus-binge ethanol diet protocol and treated by Paeonol (Pae) at 480 mg/kg. Meanwhile, RAW 264.7 cells were incubated with *C. albicans* or zymosan in the presence of 250 μg/mL laminarin (Dectin1 inhibitor) and 480 μmol/L Pae. The expressions of several critical proteins and genes of Dectin-1/TLR2/NLRP3 pathway were also examined in both animal and cell experiments. Compared with ALD mice, exogenous *C. albicans* could significantly promote the progression of ALD with aggravated pathological signs and abnormally activated liver macrophages. The mice treated with Pae could greatly reduce liver fungal capacity, the levels of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), triglyceride (TG), total cholesterol (T-CHO) content, and hepatic damage. Both in vivo and in vitro, the flamed macrophages were quenched, and the expression of proteins and genes of Dectin-1/TLR2/NLRP3 pathway were inhibited to some extent after Pae treatment compared with the ALD mice with *C. albicans* or zymosan intervention. Introgastric administration of *C. albicans* can worsen alcohol-induced liver damage via liver-intestine axis. Whereas Pae can reduce the injuries of ALD with *C. albicans* intervention, and the potential underlying mechanism might involve the Dectin-1/TLR2/NLRP3 pathway.**

RESUMEN. La enfermedad hepática alcohólica (EHA) es causada por el consumo prolongado de alcohol y está asociada con los cambios en la composición de la micobiota intestinal, especialmente *Candida albicans*. La terapia farmacológica para mejorar el desequilibrio ecológico intestinal se está convirtiendo en una estrategia prometedora para el tratamiento de la ALD. Se estableció un modelo de ALD inducido por *C. albicans* en ratones C57BL/6 usando un protocolo de dieta de etanol crónico más atracones bien definido y tratados con Paeonol (Pae) a 480 mg/kg. Mientras tanto, las células RAW 264.7 se incubaron con *C. albicans* o zymosan en presencia de 250 μg/mL de laminarina (inhibidor de Dectin1) y 480 μmol/L de Pae. Las expresiones de varias proteínas y genes críticos de la vía Dectin-1/TLR2/NLRP3 también se examinaron en experimentos con animales y células. En comparación con los ratones ALD, *C. albicans* exógena podría promover significativamente la progresión de ALD con signos patológicos agravados y macrófagos hepáticos anormalmente activados. Los ratones tratados con Pae podrían reducir en gran medida la capacidad fúngica del hígado, los niveles séricos de alanina aminotransferasa (ALT), aspartato aminotransferasa (AST), triglicéridos (TG), contenido de colesterol total (T-CHO) y daño hepático. Tanto *in vivo* como *in vitro*, los macrófagos flameados se extinguieron y la expresión de proteínas y genes de la vía Dectin-1/TLR2/NLRP3 se inhibieron hasta cierto punto después del tratamiento con Pae en comparación con los ratones ALD con intervención de *C. albicans* o zymosan. La administración introgástrica de *C. albicans* puede empeorar el daño hepático inducido por el alcohol a través del eje hígado-intestino. Mientras que Pae puede reducir las lesiones de ALD con la intervención de *C. albicans*, y el mecanismo subyacente potencial podría involucrar la vía Dectin-1/TLR2/NLRP3.

KEY WORDS: alcoholic liver disease, *Candida albicans*, paeonol.

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