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Commentary: Ex vivo perfusion with green tea

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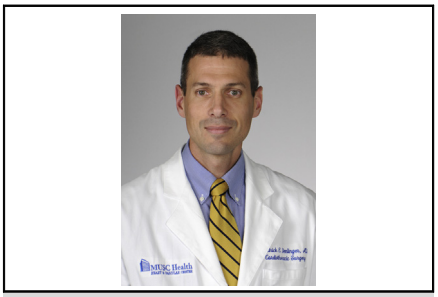

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CENTRAL MESSAGE

Triptolide has been used for centuries as an anti-inflammatory agent. It is now being explored as an EVLP adjunct medication.

Ev vivo lung perfusion (EVLP) was popularized after the initial publication from the Toronto group in 2011 in which 20 patients received marginal lungs transplants after assessment with EVLP, and the clinical outcomes were comparable to those of a contemporaneous cohort of standard lung transplants.[1] In this study, 87% of the lungs placed on the EVLP circuit were used for transplantation, which is significantly greater than the rate in other series.[2,3] Clinically, EVLP remains a tool for the evaluation of marginal lungs before committing to transplantation, whereas using EVLP for lung rehabilitation and conditioning to minimize the inflammatory reaction of reperfusion injury remains a concept of intense research interest.

Triptolide is a compound found in the root, leaf, flower, and fruit of *Tripterygium wilfordii* and has been recognized as a medicinal compound with anti-inflammatory and immunosuppressive properties for centuries.[3] It has been used in traditional Chinese medicine and is an active component of Chinese herbal tea. Numerous studies have investigated the efficacy of triptolide in cancers, including lung, colon, liver, and pancreatic. The majority of these investigations have focused on its anti-inflammatory properties and inhibition of nuclear factor-κB. Other investigations have explored the impact of triptolide on pulmonary fibrosis and how this compound interacts with inflammatory cells and fibroblasts.[4] For these reasons, using triptolide as an anti-inflammatory additive in the EVLP circuit is intriguing. Burki and colleagues[5] demonstrate significant reduction in numerous inflammatory cytokines commensurate with improved oxygenation and pulmonary vascular resistance after the addition of triptolide to the EVLP circuit.

To date, triptolide has not entered the realm of clinical pharmacology for several reasons, including the limited oral bioavailability and water solubility. Other limitations include a lack of understanding of the precise mechanism of action for any of its medicinal properties and limited natural supply of the compound. It is safe for human consumption, at least in small quantities, as noted by the fact that it is a component of green tea, which has been consumed for centuries. Considering each of these features, triptolide may hold some promise as an anti-inflammatory agent that successfully dampens the injury of ischemia and reperfusion of lungs on the EVLP circuit.

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References

1. Cypel M, Yeung JC, Liu M, Anraku M, Chen F, Karolak W, et al. Normothermic ex vivo lung perfusion in clinical lung transplantation. *N Engl J Med*. 2011;364:1431-40.
2. Fisher A, Andreasson A, Chrysos A, Lally J, Mamasoula C, Exley C, et al. An observational study of donor ex vivo lung perfusion in UK lung transplantation: DEVELOP-UK. *Health Technol Assess*. 2016;20:1-276.
3. Fan D, He X, Bian Y, Guo Q, Zheng K, Zhao Y, et al. Triptolide modulates TREM-1 signal pathway to inhibit the inflammatory response in rheumatoid arthritis. *Int J Mol Sci*. 2016;17:498.
4. Chen C, Yang S, Zhang M, Zhang Z, Zhang SB, Wu B, et al. Triptolide mitigates radiation-induced pneumonitis via inhibition of alveolar macrophages and related inflammatory molecules. *Oncotarget*. 2017;8:45133-42.
5. Burki S, Noda K, Philips BJ, Velayutham M, Shiva S, Sanchez PG, et al. Impact of triptolide during ex vivo lung perfusion on grafts after transplantation in a rat model. *J Thorac Cardiovasc Surg*. 2021;161:e65-74.