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## Paeoniflorin increases the adhesion of trophoblast to the endometrium by upregulating the expression of Integrin $\alpha V\beta 3$ and $\alpha V\beta 5$

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Successful implantation requires uterine receptivity which is determined by diverse biological factors such as adhesion molecules, cytokines, growth factors, and receptors. In our previous study, water extract of Paeonia lactiflora enhanced embryo implantation in vitro and in vivo via induction of the leukemia inhibitory factor (LIF)dependent expression of Integrin  $\alpha V\beta 3$  and  $\alpha V\beta 5$ . To investigate which one is the major component, we performed high-performance liquid chromatography (HPLC) analysis. Next, we tested these five compounds to confirm whether these single compounds enhance the adhesion of human trophectoderm-derived JAr cells to the endometrial Ishikawa cells. In addition, we checked the expression of adhesion molecules in mRNA and protein levels and performed in vivo study using the implantation failure model mice by treating RU-486. Paeoniflorin, the most abundant molecule among tested five major compounds of *P. lactiflorg*, showed enhancing effect on cellular interaction between JAr and Ishikawa cells. Paeoniflorin increased the expression of Integrin  $\alpha V\beta 3$  and  $\alpha V\beta 5$  in LIF-dependent manner. Furthermore, in vivo study showed that paeoniflorin significantly improved the number of implantation embryos. Therefore, our results suggest that paeoniflorin, a major compound of P. *lactoflora*, is a potent agent for enhancing endometrial receptivity.

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