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AIMS: The estrogenic effect of marijuana use has been investigated for the last decades; however, few studies have previously examined the effects of marijuana smoke condensate (MSC) on uterotrophic response. Furthermore, the causative chemicals for its estrogenicity have not been determined yet. Therefore, this study aimed to provide back ground information on a risk of smoking marijuana by investigating the ability of MSC to induce the estrogenic effect and identifying possible causative ingredients.

METHODS: The estrogenic effect of MSC was evaluated using the enhanced uterotrophic assay. To identify the constituents of MSC responsible for the estrogenicity, MSC was fractionated and the estrogenic activities of the seven fractionated samples were traced by the human breast cancer cell proliferation assay. Moreover, the possible causative ingredients in the fraction showing the strongest estrogenic activity were identified using GC-MS. The Bio-EEQ and I-EEQ of MSC were also calculated.

RESULTS: The treatment of 10 and 25 mg/kg MSC significantly induced uterine response, and 10 mg/kg MSC demonstrated an obvious change in the uterine epithelial cell appearance. MSC also enhanced the IGFBP-1 gene expression in a dose dependent manner. In the organic acid fraction that showed the strongest estrogenic activity among the seven fractions of MSC, phenols were identified. The Bio-EEQs of MSC and the organic fraction were 9.72 and 18.1 ng/g, respectively, and the I-EEQ of MSC was 4.24 ng/g.

CONCLUSIONS: Our results suggest that marijuana abuse is considered an endocrine-disrupting factor. Furthermore, these results point out a role for phenols in the estrogenic effect of MSC.

KEYWORDS: *Marijuana smoke condensate, Estrogenic effect, Uterotrophic assay, Phenols*

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