**Abstract**

Wallflower (*Erysimum cheiri* (L.) Crantz) belonging to the family Brassicaceae is a well-known medicinal herb in Persian medicine. Several cardiotonic steroids have isolated from different parts of this plant. The intravaginal dosage forms of wallflower have been frequently used for uterotonic purposes in traditional medicine. Accordingly, the present study explores the most frequent indications of wallflower through the history, and suggests a pharmacological hypothesis about the intravaginal delivery of this cardiotonic steroid containing herb. In this regard, study was done by searching via electronic databases and search engines including ScienDirect and Scopus, Medline/Pubmed, and Google Scholar. Information on traditional indications of the herb was extracted from the major traditional medicine manuscripts. As the result, the historical survey and the pharmacological evidences have supported the hypothesis that the inhibitory effects of wallflower cardiotonic steroids on the Na\(^+\) K\(^+\) ATPase pumps of the myocytes could affect the local vasoconstriction resulting the hypoxia, ischemia and contraction of the uterine tissue. It is suggested that more experimental studies be directed on the efficacy and safety of cardiotonic steroids of wallflower to induce uterine contractility.

**Keywords:** Wallflower, *Erysimum cheiri*, Cardiotonic steroid, Uterotonic.

1. Introduction

Wallflower (*Erysimum cheiri* (L.) Crantz) from the family Brassicaceae is a well-known Persian medicinal plant which is rich in cardiotonic steroid (CTS) compounds. This herb has been frequently used as a uterotonic remedy in traditional medicine (1, 2). Generally, CTS has a target site on Na\(^+\), K\(^+\) ATPase pump which is responsible for positive inotropic and negative chronotropic effects on the heart (3, 4). Some experimental studies have shown the similarity of the uterus physiology to that of the heart. In addition, cardiac aglycones as active moieties of the cardiac glycosides are structurally similar to the sex hormones affecting the uterus (5). Several types of CTSs have been extracted from different parts of wallflower herb (1, 2, 6-8). However, the uterotonic indications (emmenagoue, abortifacient and labor inducer properties) of the intravaginal formulations of wallflower have been frequently reported in Persian medicine (PM) manuscripts (7-11). Present work suggests a pharmacological hypothesis concerning the role of CTS content of wallflower in its frequent uterotonic indications in traditional medicine.
2. Material and methods

This study was done by searching the terms: cardenolide, cardiotonic steroid, uteroton-ic, Erysimum cheiri and wallflower via electronic databases including Sciencedirect and Scopus, and search engines of Medline/Pubmed, and Google Scholar. Information on traditional indications of wallflower was extracted from the major PM manuscripts including Al-Abnia, Al-Mansouri, Al-Hawi, Ikhtiarat Badiee, Tohfa-al Momenin, Qarabdin Salehi, Makhzn-al-Advieh, Qarabadin Kabir and Mohit Azam. Other traditional manuscripts were also used as follow: De Materia Medica, Kitab fi al-Adwiyah al-Mufradah, Al-Shamel, Kitab al-Jami li-Mufradat al-Adwiyawa al-Aghdhiya and Hadiqat al-Azhar fi Mahiyat al Ushbwal-Aqqar (12).

3. Results

The traditional indications (from 1st AD to 19th AD) of different dosage forms of wallflower have been summarized in figure 1.

As the figure demonstrates, wallflower seed (oral decoction/ vaginal suppository/ vaginal sitz bath) has been widely administered for uteroton-tic purposes (e.g., abortifacient, emmenagogue, and labor inducer). Vaginal suppository including pessary and cotton-load / sitz bath (of seed/ root/ flower) has been widely prescribed for abortifacient and emmenagogue properties. Also, vaginal sitz bath (of seed/ root/ flower) has been widely used for abortifacient, emmenagogue and anti-endometriosis properties (12).

In the second part of this study, we hypothesized that intravaginal administration of wallflower preparations being rich in CTSs could have inhibitory effects on Na+, K+ ATPase pump that is responsible for the uterine smooth muscle contraction and local vasoconstriction. This action results in the hypoxia and local ischemia, contributed to increasing intracellular calcium and production of excitatory prostaglandin, respectively. The present hypothesis recommends the intravaginal wallflower as a potential herbal remedy to get uterotonic outcomes (Figure 2).

4. Discussion

According to the described hypothesis in this study, CTS could inhibit the Na+K+ ATPase pump on the smooth muscle of vascular cells that triggers the higher intracellular calcium levels and the local vasoconstriction (13). On the other hand,
vasospasm of spiral arteries in the uterine tissue is believed to make a local ischemia and hypoxia, causing menstrual shedding of endometrial lining (14). Temporarily depriving of oxygen in uterine tissue can result in up-regulation of COX₂, increase prostaglandin production in smooth muscles, and increase of Ca²⁺ signaling and ionic gradient in the myometrial to induce uterine contractility (15-18). Therefore, Inhibition of Na⁺, K⁺ ATPase pump in myometrium may provide a uterotonic effect mechanistically similar to cardiotonic properties.

5. Conclusion

Wallflower (the herb rich in CTS) has been frequently used for uterotonic purposes in traditional medicine. The present study has discussed the potential pharmacological mechanisms of wallflower as a new natural remedy for further research on uterine contractility and related therapeutic outcomes.

Conflict of Interest

None declared.

6. References
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