



Herbal therapies in pregnancy: what works?

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Purpose of review

The aim of this article is two-fold: to report the prevalence of herbal products used by pregnant women and to evaluate the evidence of efficacy and safety of the most popular remedies.

Recent findings

Of the 671 articles identified, 15 randomized controlled trials (RCTs) and 16 non-RCTs were eligible. Ginger was the most investigated remedy and it was consistently reported to ameliorate nausea and vomiting in pregnancy. Although raspberry, blue cohosh, castor oil, and evening primrose oil are believed to facilitate labor in traditional medicine, very few scientific data support such indication. Moreover, they have been associated with severe adverse events. Data on the safety of *Hypericum perforatum* in pregnancy or lactation are reassuring, whereas efficacy was demonstrated only in nonpregnant individuals. There is still insufficient evidence regarding the efficacy and safety of Echinacea, garlic, and cranberry in pregnancy.

Summary

Epidemiological studies reported a wide range of use of herbal remedies in pregnancy. Too few studies have been devoted to the safety and efficacy of singular herbs. With the exception of ginger, there are no consistent data to support the use of any other herbal supplement during pregnancy. Severe adverse events have been reported using blue cohosh and evening primrose oil.

Keywords

herbal remedies, herbal supplements, herbal treatments, pregnancy

INTRODUCTION

A search of the literature in electronic databases (Medline, Amed, The Cochrane Library, and the PDR for Herbal Medicines) from 1970 to 2013, using the keywords ‘herbal treatments’, ‘herbal remedies’, ‘herbal supplements’, and ‘pregnancy’, found 703 articles, 515 of them published during 2000–2013, 156 between 1990 and 1999, 57 in the 1980s, and just 5 studies in the 1970s. This emphasizes the growing interest in the subject with the new millennium together with the increased utilization of herbal remedies by the general population [1[¶]]. As for many other complementary alternative medicines women result the major consumers [2] and it is not surprising that they could continue herbs use also during gestation [2]. Such remedies are most often used to counteract minor complaints like nausea, vomiting, constipation, anxiety, or back-ache. However, herbs are also claimed (and used) to solve urinary tract infections (UTIs) or to induce or accelerate labor [3–5].

Pregnant women are apprehensive about the potential toxicity of conventional medicines, so they use herbal products to complement or to replace them, although much current practice is

not evidence based [2,3]. Indeed, there is evidence of the negative effects associated with the use of some herbal remedies, and data on safety for their use in pregnancy are limited [6,7].

Although herbal medicines contain active constituents with pharmacological properties and possible interactions with other compounds, they are considered by women natural and safer than conventional drugs [2,5].

Another issue is that herbal products are over the counter and offer women greater independence for their health-care choices [8,9]. Hence, the majority of consumers do not disclose their use to the doctor and rely on family and friends or websites for information regarding such treatments [2,8].

The aim of this article is two-fold: to report the prevalence of herbal products used by pregnant

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KEY POINTS

- About half of pregnant women try a wide range of herbal treatments, although the efficacy and safety of such remedies are poorly known.
- Ginger relieves nausea and vomiting in pregnancy, similarly to vitamin B6 or dimenhydrinate.
- Blue cohosh and primrose oil have been associated with severe fetal complications, whereas their efficacy remains to be demonstrated.
- There is still insufficient efficacy and safety evidence supporting the clinical use of Echinacea, garlic, and cranberry.
- St John's wort use in pregnancy or lactation is reported to be well tolerated.

women and to evaluate the evidence of efficacy and safety of the most popular remedies.

METHODS

A systematic literature search was performed in October 2013 in the Medline electronic database. We performed a search about herbal treatments, their applications, and potential effects in pregnancy over the period 1990–2013.

As specified previously, the search terms were 'herbal treatments', 'herbal remedies', 'herbal supplements', and 'pregnancy'. The search was limited to articles published in the English language and those that were easily retrievable via the home library. Further relevant studies, in particular about the search of randomized controlled trials (RCTs), were located by hand searching the reference lists of the recent systematic reviews.

For inclusion, an article had to contain original data on either the prevalence of use or adverse effects of herbal treatments during pregnancy.

Only human studies were included, data from herbal treatments in combination with other herbs or multivitamins as well as animal and in-vitro investigations were excluded.

Fertility treatments, contraception, and the deliberate use of herbal medicine products as abortifacients were also excluded. Topical treatments were included.

We attempted to obtain hard copies of all the studies listed through our own university library or interlibrary loans.

Expert judgement, rather than a formal quality appraisal, was used to determine which studies were included.

In the first section, we analyzed only epidemiological data and in the second section, we examined the use and efficacy of single herbal treatments.

All sources of information were read and evaluated by one of us (G.D.), and later independently checked by another author (G.B.). Data were extracted according to the predefined criteria and are represented in different tables.

RESULTS

The decision tree used for the inclusion of the studies about the most investigated herbal products is presented in Fig. 1.

Out of the 671 articles published during the last 2 decades (1990–2013), 258 were excluded from the analysis as they described Chinese herbal remedies.

Only 15 studies reported RCTs, 14 of them have been described in detail in a previous publication [7].

The features of the single herbal treatments originating in the RCT trials are reported in Table 1 [10–24]. Moreover, efficacy and safety of single-herb remedies originating from the observational studies are described in Table 2 [25,26^a,27–40].

MOST POPULAR HERBAL REMEDIES

Twenty-two articles were screened [41–58,59^a, 60–62], 16 of them concerning only the use of herbal treatments and six pertaining the employment of complementary alternative medicines (CAM), whereas two [61,62] were excluded from this analysis because of duplicate publications.

Out of the remaining 20 studies, 13 were observational, two case–control, and five cross-sectional studies. All the studies were conducted between 1997 and 2013, and all the data were obtained from self-administered questionnaires or from a prestructured questionnaire through a face-to-face interview performed during pregnancy or 2–3 days after the delivery. Only in three cases, the questionnaire was administered by a telephone call after a variable time after delivery (from 2 weeks to 8 years).

Most of the published data were collected in Europe [46,48,54,55,59^a] or in the USA [42,43,45, 50–52].

Estimates of frequency of use of herbal treatments during pregnancy range from 0.9 [48] to 87% [41], and such differences could be related to the study designs, data collection methods, and cultural characteristics of the investigated population.

According to the results from other reviews [9,63], women using herbal remedies were more likely to be Caucasian, middle-aged, nonsmokers, and with a high level of education. Only two studies

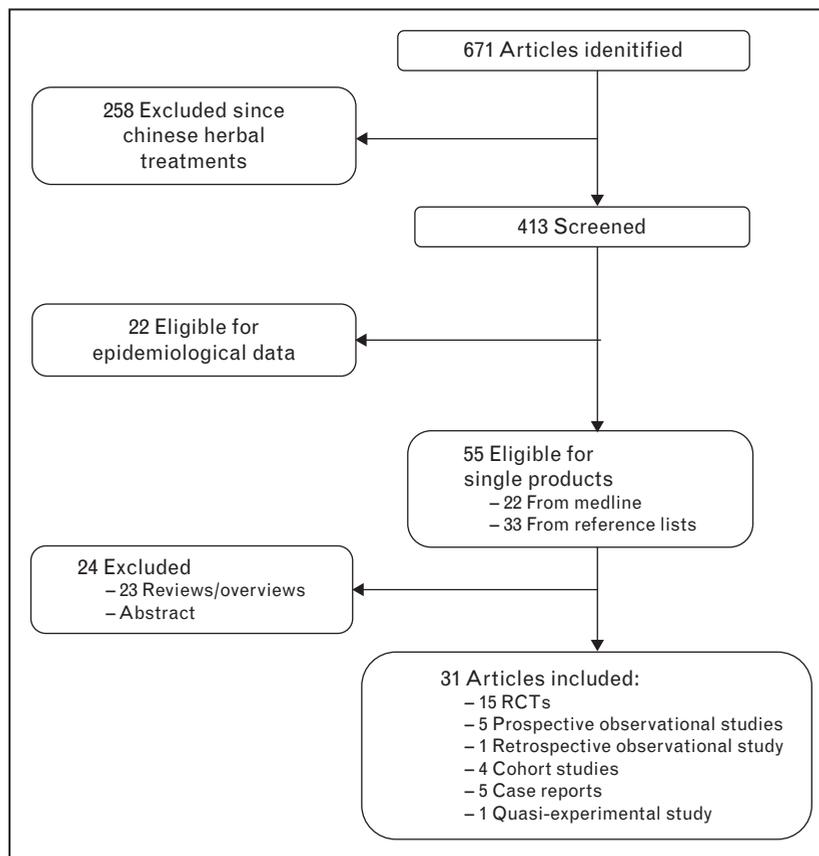


FIGURE 1. Flow chart of examined studies.

described the women's employment status [54,60] and we cannot summarize this characteristic as it is a socio-cultural feature of the population.

From the analysis of these studies, we summarize in Table 3 the 12 herbs most frequently consumed by pregnant women.

MOST INVESTIGATED HERBAL REMEDIES

We screened 391 articles describing single-herb remedies and we located other studies by hand searching the reference lists of the most recent reviews.

With this combined search, we found 15 RCTs [10–24] (Table 1), five prospective observational studies [25,28–31], one retrospective observational study [27], four cohort studies [26^a,36–38], five case reports [33–35,40], and a quasi-experimental study [39] (Table 2).

Twelve articles explored the effect of ginger [10–19,25,26^a], five studied St. John's wort [21,29–32], three investigated blue cohosh [33–35], another three castor oil [24,37,38], two evaluated raspberry leaf [22,27], two garlic [23,36], two primrose oil [39,40], and two other studies reported cranberry

and Echinacea, respectively [20,28]. Ten of the non-RCTs investigated only the safety of the herbal products [25,26^a,29–35,40].

Ginger

Ginger was thoroughly investigated in 10 RCTs [10–19], one prospective observational study [25], and one cohort study [26^a]. The primary objective of the RCTs was to investigate the effectiveness of ginger on nausea and vomiting during pregnancy, whereas the primary outcome of the observational studies was to examine the safety of this product on congenital malformations and some pregnancy outcomes. Five RCTs reported the superiority of ginger compared with placebo [10–14], whereas four other trials found ginger to be equally effective when compared to vitamin B6 [15,16,18,19] and dimenhydrinate [17].

There were no significant differences between ginger and the other treatments with respect to adverse events and no increased risk for major malformations, stillbirth/perinatal death, preterm birth, low birth weight, or low Apgar score [25,26^a].

Table 1. Results from RCTs

Herb remedy	Reference	Study design	Indication	Dose/duration	Results	Side-effects	Fetal outcomes
Ginger	[10]	Double-blind, randomized, placebo-controlled	Nausea and vomiting	Ginger: 5 g/day; Duration: 4 days	Better than placebo on nausea andretching; Equal to placebo on vomiting	Reflux, heartburn	No significant differences in birth weight, gestational age at delivery, Apgar scores, and congenital abnormalities.
	[11]	Double-masked randomized, placebo-controlled	Nausea and vomiting	Ginger: 1 g/day; Duration: 7 days	Better than placebo on nausea and vomiting	Headache, abdominal discomfort, heartburn, diarrhea	No side-effects were observed.
	[12]	Single-blind, randomized, placebo-controlled	Nausea and vomiting	Ginger: 1 g/day; Duration: 4 days	Better than placebo on nausea and vomiting	None	ND
	[13]	Double-blind, randomized, placebo-controlled	Nausea and vomiting	Ginger: 1 g/day; Duration: 2 weeks	Better than placebo on nausea and vomiting	None	ND
	[14]	Double-blind, randomized, crossover	Nausea and vomiting	Ginger: 250 mg/day; Duration: 4 days	Better than placebo on nausea and vomiting	None	ND
	[15]	Double-blind, randomized controlled	Nausea and vomiting	Ginger: 1 g/day; Duration: 4 days	Equal to vitamin B6	ND	No significant differences in abortion, birth weight, gestational age at delivery, Apgar scores, and congenital abnormalities.
	[16]	Double-blind, randomized controlled	Nausea and vomiting	Ginger: 1.05 g/day; Duration: 3 weeks	Equal to vitamin B6	Burning sensation, vomiting, and dry retching	No side-effects were observed.
	[17]	Double-blind, randomized controlled	Nausea and vomiting	Ginger: 1 g/day; Duration: 1 week	Equal to dimenhydrinate	Drowsiness and heartburn	ND
	[18]	Double-blind, randomized controlled	Nausea and vomiting	Ginger: 1.5 g/day; Duration: 3 days	Equal to vitamin B6	Sedation and heartburn	ND
	[19]	Double-blind randomized controlled	Nausea and vomiting	Ginger: 650 mg/day; Duration: 4 days	Equal to vitamin B6	Sedation, heartburn, and arrhythmia	ND
Cranberry	[20]	Randomized controlled	Urinary tract infections	Cranberry (A): 240 mg/day; Cranberry (B): 80 mg/day; Duration: until delivery	Not effective	Gastrointestinal upset	ND
St. John's wort	[21]	Double-blind, randomized, placebo-controlled	Depression	<i>Hypericum perforatum</i> : oily extract; Duration: 16 days	Effective	Irritation surgical site	NA
Raspberry leaf	[22]	Double-blind, randomized, placebo-controlled	Shorten labor	Raspberry leaf: 2.4 g/day; Duration: from 32 weeks until labor	Not effective	None	No significant differences in Apgar score at 5th min, birth weight, transfer to NICU.
Garlic	[23]	Single-blind randomized, placebo-controlled	Prophylaxis of preeclampsia	Garlic: 800 mg/day; Duration: 8 weeks	Not effective	Foul odor and nausea	No side-effects were observed.
Castor oil	[24]	Randomized controlled	Induction of labor	Castor oil: 60 ml; Duration: single dose	Effective	Nausea	No differences in Apgar scores and meconium-stained amniotic fluid.

Some data are reported from Ref. [7]. NA, not applicable; ND, not described; NICU, neonatal intensive care unit; RCTs, randomized controlled trials.

Table 2. Results from non-RCTs

Herb remedy	Reference	Study design	Clinical use	Dose/duration	Results	Maternal adverse events	Fetal outcomes
Ginger	[25] ^a	Prospective, observational	Nausea and vomiting	Dose: 1 g/day; Duration: from 4th to 14th week	Mild effect	ND	No significant differences in number of live births, spontaneous abortions, stillbirth, therapeutic abortions, gestational age at birth. There were more infants <2500 g in nonusers.
Raspberry leaf	[26] ^a [27]	Prospective cohort Retrospective, observational	Nausea and vomiting Shorten labor	ND Not applicable	Safe Not effective	Vaginal bleeding after 17 weeks None	No increased risk of malformations, stillbirth, preterm birth, low birth weight, low Apgar score. No significant differences in Apgar scores at 5th min or transfer to NICU.
Echinacea	[28]	Prospective, observational	Upper respiratory tract ailments	Dose: 250–1000 mg/day; Duration: 5 or 7 days	Effective	ND	Rate of malformations was not significantly different.
St. John's wort	[29] ^a	Prospective, observational	Depression	Dose: 615 mg/day; Duration: not applicable	Safe	None	Rate of malformations, live birth and prematurity were not significantly different.
Blue cohosh	[30] ^a [31] ^a [32] ^a	Prospective, observational Prospective, observational Case report	Depression Depression Depression	Dose: 900 mg/day; Duration: at least 4 weeks Dose: 225–2150 mg/day; Duration: 4 months (median) Dose: 900 mg/day; Duration: from 24 weeks until delivery	Safe Safe Safe	None None None	No side-effects were observed ND Birth weight, Apgar score, physical examination, laboratory results and behavior assessment at 4 and 23 days were normal.
Blue cohosh	[33] ^a	Case report	Induction of labor	Dose: ND; Duration: last 4 weeks of pregnancy	Unsafe	ND	Acute myocardial infarction, profound congestive heart failure and shock.
Garlic	[34] ^a [35] ^a	Case report Case report	Induction of labor Induction of labor	ND ND	Unsafe Unsafe	ND ND	Focal motor seizures of the right arm at 26 h of age. Severe multiorgan hypoxic injury and permanent central nervous system damage.
Garlic	[36]	Prospective cohort	Preterm birth prophylaxis	Dose: >0.4 g/day; Duration: ND	Effective	ND	ND
Castor oil	[37]	Retrospective cohort	Induction of labor	ND	Not effective; Safe	None	ND

(Continued)

Table 2 (Continued)

Herb remedy	Reference	Study design	Clinical use	Dose/duration	Results	Maternal adverse events	Fetal outcomes
	[38]	Prospective cohort	Induction of labor	Dose: 60 ml; Duration: single dose	Effective	Nausea	No differences in birth weight, Apgar scores, meconium-stained amniotic fluid respect with untreated.
Evening primrose oil	[39]	Retrospective quasi-experimental	Shorten labor	Dose: ND; Duration: last 3 weeks of pregnancy	Not effective; Unsafe	Prolonged rupture of membranes, oxytocin augmentation, arrest of descent and vacuum extraction	ND
	[40] ^a	Case report	Shorten labor	Dose: 6.5 g; Duration: 1 week	Unsafe	ND	Petechiae and ecchymosis in the newborn at 17 h of age.

ND, not described; NICU, neonatal intensive care unit; RCTs, randomized controlled trials.
^aStudies investigating safety only.

Table 3. Herbs most frequently used in pregnant women and reasons for their use (reported in alphabetical order)

Herb	Reasons for use
Almond oil	Stretch marks
Aloe	Digestive problems, constipation, capillary frailty
Chamomile	Anxiety, digestive problems, relax, sleep
Cranberry	Treat and prevent urinary tract infections
Echinacea	Common cold, strengthen immune system
Fennel	Fluid retention
Ginger	Nausea, vomiting
Peppermint	Indigestion/heartburn, nausea/morning sickness
Raspberry leaf	Induce and ease labor
St. John’s wort	Depression
Teas/green tea	Anxiety, digestive problems, constipation
Valerian	Anxiety

Raspberry

The use of raspberry to induce and ease labor was described in one RCT [22] and one retrospective observational study [27]. In both the studies, raspberry did not shorten the first stage of labor. The only clinically significant finding was the shortening of the second stage of labor with lower rate of forceps deliveries compared with placebo.

The use of raspberry was not associated with maternal–fetal adverse events.

St. John’s wort

There were four observational studies regarding the use of St. John’s wort in the treatment of mild and moderate depression [29–32], two of them were conducted during pregnancy [29,32] and two during lactation [30,31]. The purpose of these studies was to determine whether exposure to this agent in pregnancy was associated with major fetal malformations or with infant adverse events. The use of St. John’s wort was found to be well tolerated in both conditions. Only one RCT [21] was performed to determine the effects of a topical preparation on cesarean wound healing. At 10th day postpartum, St John’s wort facilitated cesarean wound healing and minimized the formation of scar. In addition, significantly lower pain and pruritus were reported by the treatment group at the 40th day postpartum.

Garlic

One RCT [23] analyzed the effects of garlic on the prevention of preeclampsia in high-risk women. There was a reduction in the total cholesterol level, whereas neither hypertension nor preeclampsia was reduced.

Minor adverse events such as a foul odor and nausea were reported in the garlic users, no effect was found on neonates.

One observational cohort study [36] demonstrated that garlic intake was associated with a lower risk of both early and late preterm delivery. Maternal–fetal adverse events were not analyzed.

Cranberry

Only one RCT [20] compared cranberry extract with placebo in the prevention of UTIs. A non-significant reduction in the frequency of both asymptomatic bacteriuria and UTIs was reported in women receiving cranberry. The study, however, was not sufficiently powered to detect such a difference. Moreover, 38.8% of the participants withdrew, mostly because of gastrointestinal upset. There was no difference between groups with respect to obstetric and neonatal outcomes.

Blue cohosh

This remedy is expected to induce and accelerate labor.

Only three case reports are available and they described cardiovascular side-effects using blue cohosh at the time of delivery [33–35]. In one case, the neonate experienced acute myocardial infarction, profound congestive heart failure, and shock [33]; in another case, there was a severe multi-organ hypoxic injury [35]; and in the last one, perinatal stroke occurred [34].

No studies are available on efficacy.

Echinacea

One prospective observational study [28] evaluated the safety and the efficacy of Echinacea when used during the first trimester for upper respiratory tract ailments. No increased risk of major malformations was reported. Respiratory symptoms improved with respect to nontreated group.

Castor oil

There were two observational studies [37,38] and one RCT [24] about the effect of castor oil on the induction of labor. The RCT showed a significant increase in labor initiation in the treated group compared with controls and the same outcome was found in the prospective study by Garry *et al.* [38]. However, in the study by Boel *et al.* [37], castor oil showed no effect on the time of birth. Nausea was the most common maternal side-effect reported.

There were no data on neonatal mortality or morbidity.

Evening primrose oil

Evening primrose oil is a fatty acid used to trigger cervical ripening.

In a retrospective study of quasi-experimental design [39], this product did not shorten gestation or decrease the overall length of labor; moreover, it increased the incidence of prolonged rupture of membranes, oxytocin augmentation, arrest of descent, and vacuum extraction.

There was one case of petechiae and ecchymosis in a newborn, whose mother took primrose oil a week before giving birth [40].

CONCLUSION

Epidemiological studies on the use of herbal remedies in pregnancy reported a wide range of use. However, some of these studies are limited by methodological flaws (lack of prestructured questionnaires/interviews, recall bias, etc.). Excluding them, it is reasonable to conclude that the consumption of herbal remedies during pregnancy ranges from 27 to 57% in Europe and from 10 to 73% in the USA.

Anxiety is one of the most frequent reasons for use. Indeed, there are at least three herbs claimed as anxiety relievers, that is, chamomile, teas, and valerian. For none of them is there a scientific demonstration of efficacy, apart from the traditional beliefs.

On the contrary, the popular use of ginger for the relief of hyperemesis gravidarum has been substantiated by clinical trials which demonstrated the antiemetic effect of ginger also in a number of other clinical indications, including chemotherapy-induced nausea [64], motion sickness [65,66], and postoperative nausea [67,68].

The active compound allowing the antinausea and antiemetic mechanism of ginger has not been fully identified, and it has variously been attributed to the gingerols, shogaol, or zingiberene content. Mechanism of action included serotonin antagonism and vasopressin suppression to reduce tachygastric activity and to be weakly cholinergic [69].

Some studies in nonpregnant women show that ginger has an anticoagulant effect and women taking anticoagulant therapy should avoid it completely [70,71]. Furthermore, ginger is known to be a stomach irritant, and stimulates the secretion of bile being contraindicated in people with a history of gallstones [72]. Finally, it should be avoided in

women with diabetes mellitus, who are controlled through oral antidiabetics or insulin [73] and it may cause hypotension [69].

Although raspberry, blue cohosh, castor oil, and evening primrose oil are believed to facilitate labor in traditional medicine, very few scientific data are available to support such indication. Raspberry leaf as well as evening primrose oil has proven ineffective, the latter arising doubts about safety. Labor induction with castor oil seems promising and further studies will help to comprehend the available contrasting data.

Of paramount importance is the alarm signal toward blue cohosh. Efficacy as labor stimulant is lacking, although a significant number of U.S. midwives use it [74]. On the contrary, three case reports describe significant adverse events in neonates whose mother received the herb remedy [33–35].

The efficacy of St John's wort in the treatment of mild-to-moderate depression has been assessed in nonpregnant women and men [75]. Current evidence suggests that at least two of the herb constituents, hypericin and hyperforin, play a significant role in this pharmacologic effect [76,77]. Data on its use in pregnancy or lactation reassure about safety, whereas efficacy was not specifically reported.

There is still insufficient evidence to make any conclusions regarding Echinacea, garlic, and cranberry in pregnancy, although the efficacy of the latter in preventing the recurrence of UTIs has been well demonstrated in nonpregnant women [78].

Furthermore, it is necessary to highlight the adverse events associated with the prolonged use of almond oil. Despite the absence of studies devoted to this compound, in a survey performed in postpartum women it was found that those who applied almond oil to their abdomen daily (to avoid stretch marks) were at higher risk for preterm delivery [59*].

In conclusion, despite the very large popular use of herbal remedies during pregnancy, there are very few studies that have been devoted to the specific evaluation of these treatments. With the exception of ginger supplementation for hyperemesis gravidarum, there is actually no clinical indication for the use of any other herbal treatment in pregnant women. Vice versa, caution on the use of several compounds because of poor safety is available from case reports and epidemiological studies.

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None.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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- of special interest
- of outstanding interest

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