Appendix 1. Critical Appraisal Tables

Interventional studies
(n = 29)

Ref#	First author	Year	Study period (MM/YY)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	TOTAL (x/17)
(80)	**Akbari**	2015	12/13 - 06/14	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	11
(56)	**Asgharikhatooni**	2015	2013 - 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	15
(81)	**Basirat**	2009	2005 - 2006	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes	No	Yes	12
(82)	**Biswas**	2011	11/04 – 04/05	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes	11
(83)	**Chittumma**	2007	05/05 – 08/05	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes	No	Yes	12
(57)	**Chu and Shen**	2008	Not reported	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	16
(58)	**Ensiyeh**	2009	04/06 – 07-06	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	14
(84)	**Firouzbakht**	2014	Not reported	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes	No	No	10
(101)	**Fischer-Rasmussen**	1990	1986 -1988	Yes	No	No	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	No	Yes	No	No	8
(59)	**Gharabaghi**	2011	07/09 – 05/10	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	14
(102)	**Huang**	2000	07/96 – 10/97	Yes	No	No	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	9
(85)	**Jafari-Dehkordi**	2017	03/13 – 08/13	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	12
(60)	**Kalati**	2018	03/14 – 08/15	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	15
(61)	**Kalava**	2013	06/10 – 04/11	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	16

1. Was the study setting adequate? 2. Was the sample calculation reported? 3. Was the study population described? 4. Were the intervention and control described? 5. Was the control adequate for the study? 6. Was the randomisation process described? 7. Was blinding described? 8. Was blinding appropriate? 9. Were both study groups treated the same? 10. Is intention to treat described? 11. Was direct statistical analysis performed? 12. Were the study outcomes validated? 13. Were the study outcomes clinically relevant? 14. Was follow-up time sufficient? 15. Were all participants accounted for at the end of the study? 16. Were all important outcomes considered? 17. Are the study results generalizable?

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Ref#	First author	Year	Study period (MM/YY)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	TOTAL (x/17)
(86)	**Ketsuwan**	2018	07/16 - 10/17	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	13
(103)	**Kohama**	2006	Not reported	Can't tell	No	No	Yes	No	No	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	8
(104)	**Ozalkaya**	2018	11/10 - 06/11	Yes	No	Yes	Yes	Yes	No	No	No	Yes	No	Yes	No	Yes	No	Yes	No	No	8
(87)	**Pongrojpaw**	2012	01/05 -12/05	Yes	No	Yes	Yes	No	No	No	No	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	10
(105)	**Rukh**	2016	06/12 – 05/13	Yes	No	No	Yes	No	No	No	No	Yes	No	No	Yes	Yes	Yes	Yes	No	No	7
(62)	**Sadi**	2016	05/13 – 07/13	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	16
(63)	**Shahrahmani**	2018	06/15 - 02/16	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	16
(64)	**Simpson**	2001	05/99 – 02/00	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	14
(88)	**Smith**	2004	07/00 – 03/02	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	12
(65)	**Tabeshpour**	2017	10/15 - 02/16	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	16
(66)	**Tianthong**	2018	06/16 – 06/17	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	16
(67)	**Vutyavanich**	2001	10/98 – 02/99	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes	14
(68)	**Wagner**	2018	03/12 - 03/16	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Ye3s	Yes	Yes	Yes	Yes	Yes	16
(89)	**Willetts**	2003	03/99 – 11/99	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	No	Yes	No	Yes	13
(69)	**Yuan**	2016	04/12 – 06/12	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	16
																				Average	**12.76**

1. Was the study setting adequate? 2. Was the sample calculation reported? 3. Was the study population described? 4. Were the intervention and control described? 5. Was the control adequate for the study? 6. Was the randomisation process described? 7. Was blinding described? 8. Was blinding appropriate? 9. Were both study groups treated the same? 10. Is intention to treat described? 11. Was direct statistical analysis performed? 12. Were the study outcomes validated? 13. Were the study outcomes clinically relevant? 14. Was follow-up time sufficient? 15. Were all participants accounted for at the end of the study? 16. Were all important outcomes considered? 17. Are the study results generalizable?

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Observational studies
(n = 27)

Ref#	First author	Year	Study period (MM/YY)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	TOTAL (x/14)
(90)	Ács	2009	1980 - 1996	Retro	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Yes	10
(24)	Bettinol	2018	02/12 – 10/17	Xsect	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes	No	No	7
(70)	Choi	2015	Not reported	Pro	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	11
(92)	Chuang	2006a	1985 - 1987	Pro	No	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	No	9
(91)	Chuang	2006b	09/84 – 06/87	Xsect	No	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	No	8
(71)	Colapinto	2015	2008 - 2011	Pro	No	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	11
(93)	Cuzzolin	2010	01/10 - 10/09	Retro	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	10
(94)	Facchinetti	2012	Not reported	Retro	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	10
(95)	Gallo	2000	1996 - 1998	Pro	No	No	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	Yes	8
(73)	Heitmann	2016	1999 - 2006	Pro	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	12
(72)	Heitmann	2013a	1999 -2006	Pro	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	12
(74)	Heitmann	2013b	1999 - 2006	Pro	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	12
(14)	Holst	2008	1995 - 2004	Pro	No	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	10
(75)	Kolding	2015	1996 - 2003	Pro	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	12

1. Prospective, retrospective or cross-sectional? 2. Was the sample calculation reported? 3. Was the study population described?
4. Was an unexposed comparator included in the study? 5. Were the cases and comparators recruited from the same population?
6. Were the cases and comparators recruited in the same way? 7. Were inclusion and exclusion criteria stated for cases?
8. Were inclusion and exclusion criteria stated for comparators? 9. Was exposure validated? 10. Were the study outcomes validated? 11. Were all relevant confounders accounted for? 12. Were the statistical analyses adequate? 13. Were the study outcomes measured objectively? 14. Was follow-up time sufficient?

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Ref#	First author	Year	Study period (MM/YY)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	TOTAL (x/14)
(106)	**Mabina**	1997	1994	Xsect	No	Yes	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	No	7
(76)	**McLay**	2017	2012	Xsect	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	11
(31)	**Moussally**	2009	1998 - 2003	Pro	No	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	Yes	10
(34)	**Nordeng**	2011	Not reported	Xsect	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	11
(77)	**Plangger**	2005	01/20 – 12/03	Retro	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	12
(96)	**Portnoi**	2003	Not reported	Pro	No	No	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes	9
(78)	**Räikkönen**	2010	03/98 -11//98	Pro	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	12
(79)	**Räikkönen**	2017	2009 - 2011	Pro	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	12
(97)	**Strandberg**	2001	03/98 - 11/98	Retro	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	10
(98)	**Strandberg**	2002	2000 - 2001	Retro	No	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	9
(99)	**Trabace**	2015	2010 - 2013	Retro	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	10
(100)	**Zamawe**	2018	2005 -2010	Retro	No	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	10
																	Average	10.2

1. Prospective, retrospective or cross-sectional? 2. Was the sample calculation reported? 3. Was the study population described?
4. Was an unexposed comparator included in the study? 5. Were the cases and comparators recruited from the same population?
6. Were the cases and comparators recruited in the same way? 7. Were inclusion and exclusion criteria stated for cases?
8. Were inclusion and exclusion criteria stated for comparators? 9. Was exposure validated? 10. Were the study outcomes validated? 11. Were all relevant confounders accounted for? 12. Were the statistical analyses adequate? 13. Were the study outcomes measured objectively? 14. Was follow-up time sufficient?

Case Reports
(n = 19)

Ref#	First author	Year	1	2	3	4	5	6	7	8	TOTAL (x/8)
(109)	Akita	2003	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
(107)	Al-Jaroudi	2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
(114)	Bentele-Jaberg	2015	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
(38)	Blitz	2016	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
(110)	Cheang	2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
(115)	Dag	2014	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
(37)	Finkel	2016	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
(108)	Hauksdottir	2014	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
(120)	Mann	2004	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
(111)	Ozturk	2018	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
(119)	Roulet	1988	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
(41)	Shamshirsaz	2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
(116)	Silva	2017	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	7
(121)	Sridharan	2009	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
(112)	Stavropoulos	2018	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
(40)	Tait	2002	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
(113)	Thomas	1998	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
(39)	Wong	2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
(117)	Zengin	2015	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7

1. Were the patient's demographic characteristics clearly described? 2. Was the patient's history clearly described and presented as a timeline?
3. Was the clinical condition of the patient on presentation clearly described? 4. Were diagnostic tests or assessment methods and the results clearly described?
5. Was the intervention(s) or treatment procedure(s) clearly described? 6. Was the post-intervention clinical condition clearly described?
7. Were adverse events (harms) or unanticipated events identified and described? 8. Does the case report provide takeaway lessons?

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Appendix 2. Types of Studies Included in Systematic Review

Interventional studies						References
	Triple-blind	Double-blind	Single-blind	Unclear		
Positive-controlled	1	3	1	5	9	(58,80,82,83,85,87,88,103,105)
Placebo-controlled		14	1	2	18	(56,57,59-69,86,89,102,104)
Positive & Placebo controlled		0	0	1	1	(84)
Crossover		0	0	1	1	(101)
Observational studies						
	Prospective		Retrospective			
Case-control studies	1				1	(90)
Cohort studies	12		8		20	(14,31,70-75,77-79,92-100)
Cross-sectional surveys	5				5	(24,34,76,91,106)
Case reports	19				19	(37-41,107-117,119-121)
				TOTAL	**74**	

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Appendix 3. Adverse Events During Pregnancy and the Postnatal Period

#	Reference	Study type	Herbal medicinal product	Incidence	Nature
(90)	**Ács *et al.*, 2009, Hungary**	Case-control study	**Senna**	Not applicable	Polyhydramnios (OR 3.8, 95% CI 1.6, 8.9), influenza/ common cold (OR 1.9, 95% CI 1.5, 2.4), and acute digestive maternal diseases (OR 1.8, 95% CI1.2, 2.89) were reported associated with senna treatment during pregnancy
(80)	**Akbari *et al.*, 2015, Iran**	Positive-control randomized trial (oxytocin)	**Dill**	Not applicable	No maternal or fetal adverse events were observed with dill consumption
(109)	**Akita, 2003, USA**	Case report	**Arrowroot**	Not applicable	Generalized erythematous papular rash
(107)	**Al-Jaroudi *et al.*, 2016, Saudi Arabia**	Case report	**Myrrh**	Not applicable	Abdominal pain, nausea and vomiting for 2 days
(56)	**Asgharikhatooni *et al.*, 2015, Iran**	Placebo-controlled double-blind randomized trial	**Horsetail**	39.1%	14.8 % difficulty walking, 5.6 % fever, 5.6 % paresis, 3.7 % urination frequency, 3.7 % nausea, 1.9 % vomiting, 1.9 % diarrhea, 1.9 % skin problems
(81)	**Basirat *et al.*, 2009, Iran**	Placebo-controlled double-blind randomized trial	**Ginger**	6.2%	Dizziness and heartburn, minor
(114)	**Bentele-Jaberg *et al.*, 2015, Switzerland**	Case report	**Fenugreek**	Not applicable	Toxic epidermal necrolysis: fever, headache, bullous exanthema, skin erosions
(24)	**Bettiol *et al.*, 2018, Italy**	Cross-sectional online survey	**All CAMs**	6.90%	Diarrhea, tachycardia, cutaneous rash

(82)	**Biswas *et al.*, 2011, India**	Positive-control single-blind randomized trial (doxylamine 10 mg, pyridoxine 10 mg)	**Ginger**	< 1 %	Body ache, loose stools, moderate
#	**Reference**	**Study type**	**Herbal medicinal product**	**Incidence**	**Nature**
(38)	**Blitz *et al.*, 2016, USA**	Case report	**Black cohosh**	Not applicable	Severe hyponatremia (114 mmol/L)
(110)	**Cheang *et al.*, 2016, USA**	Case report	**Raspberry leaf**	Not applicable	Hypoglycemia
(83)	**Chittumma *et al.*, 2007, Thailand**	Positive-control double-blind randomized trial (Vitamin B6)	**Ginger**	25.4%	12.7% heartburn, 11.1% sedation, 1.6% arrhythmia, minor
(70)	**Choi et al., 2015, Republic of Korea**	Cohort study Prospective	**Ginger**	3.3%	Marginally increased percentage of stillbirths and admissions to NICU in case group ($p = 0.05$ and $p = 0.07$, respectively), compared to controls
(57)	**Chu and Shen, 2008, China**	Placebo-controlled double-blind randomized trial	**Red sage**	Not applicable	No adverse evets were reported for treated patients
(92)	**Chuang *et al.*, 2006a, Taiwan**	Cohort study Prospective	**Huang Lian**	Not applicable	LBW (OR: 1.42; CI: 0.65, 3.10) and SGA babies (OR: 1.32; CI: 0.82, 2.12) reported if *Rhizoma coptidis* was used > 56 times
(91)	**Chuang et al., 2006b, Taiwan**	Cross-sectional analysis	**All HMPs**	Not applicable	**Huang Lian** during the 1st trimester - congenital malformations of the nervous system (AOR 8.62, 95% CI 2.54, 29.24) and the external genital organs (AOR 3.82, 95% CI 1.18, 12.40). **An-tai-yin** during the 1st trimester - malformations of the musculoskeletal and connective tissue (AOR 1.61, 95% CI 1.10, 2.36), and the eye (AOR 7.30, 95% CI 1.47, 36.18)

(71)	**Colapinto *et al.*, 2015, Canada**	Cohort study Prospective	**Regular, green and herbal teas**	Not applicable	No significant associations were found between tea intake and adverse birth outcomes or increased concentrations of organophosphate and organochlorine pesticides
(93)	**Cuzzolin *et al.*, 2010, Italy**	Cohort study Retrospective	**All**	3.7%	0.9 % constipation (**polyherbal tisane**), 2.8 % itching and rash (**aloe or almond oil**)
#	**Reference**	**Study type**	**Herbal medicinal product**	**Incidence**	**Nature**
(115)	**Dag *et al.*, 2014, Turkey**	Case report	**Mountain germander**	Not applicable	Hepatotoxicity requiring hospitalization
(58)	**Ensiyeh *et al.*, 2009, Iran**	Positive-control double-blind randomized trial (Vitamin B6)	**Ginger**	Not applicable	No adverse events or adverse birth outcomes were reported for ginger
(94)	**Facchinetti *et al.*, 2012, Italy**	Cohort study Retrospective	**All**	1.3%	1% rash and itching (**almond oil or aloe**), 0.3% constipation (**polyherbal tisane**). Regular use of **almond oil** was associated with PTB (OR = 2.09; 95% CI: 1.07–4.08, p = 0.030) and **chamomile** with LBW infants (OR = 2.1; 95% CI: 0.99–4.60, p = 0.052), compared to non-users
(37)	**Finkel and Zarlenko, 2004, USA**	Case report	**Blue cohosh**	Not applicable	Neonatal ischemic stroke
(101)	**Fischer-Rasmussen *et al.*, 1990, Denmark**	Cross-over trial	**Ginger**	Not applicable	No adverse events were observed
(84)	**Firouzbakht *et al.*, 2014, Iran**	Placebo and positive-control double-blind randomized trial (Vitamin B6)	**Ginger**	27.6%	10.2% stomach-ache, heartburn, increased nausea

(95)	**Gallo *et al.,* 2000, Canada**	Cohort study Prospective	**Echinacea**	3.1%	Inguinal hernia, hydronephrosis, syndactyly, duplicate renal pelvis, laryngotracheomalacia, trisomy 18
(59)	**Gharabaghi *et al.,* 2011, Iran**	Placebo-controlled double-blind randomized trial	**Rosehip extract**	Not reported	Vomiting, nausea, urinary frequency
#	**Reference**	**Study type**	**Herbal medicinal product**	**Incidence**	**Nature**
(108)	**Hauksdottir *et al.,* 2015, Iceland**	Case report	**Licorice**	Not applicable	Severe, very early onset pre-eclampsia
(73)	**Heitmann *et al.,* 2016, Norway**	Cohort study Prospective	**Echinacea**	1.5%	Hypospadias, cleft lip, hypoplastic left heart syndrome. No increased odds of malformations overall (AOR 1.1, 95% CI 0.6, 2.1) major malformations (AOR 0.6, 95% CI 0.2 - 1.8) or cardiac malformations (AOR 0.6, 95% CI 0.1 - 4.3)
(72)	**Heitmann *et al.*, 2013a, Norway**	Cohort study Prospective	**Cranberry**	9.7%	Bleeding (spotting) in 2nd and 3rd trimesters if used after 17 WKP
				5.8%	Hypospadias, macrocephaly, deformity of the sternocleidomastoid muscle, congenital hip dislocation, ankyloglossia, undescended testicle. No increased odds of overall malformations (AOR 1.1, 95% CI 0.8 - 1.7) or major malformations (AOR 0.7, 95% CI 0.4 - 1.3)
(74)	**Heitmann *et al.*, 2013b, Norway**	Cohort study Prospective	**Ginger**	7.8%	Bleeding (spotting) after week 17. 7.8% users vs. 5.8% non-users (p = 0.007). No increased odds of congenital malformations
(14)	**Holst *et al.,* 2009, Norway**	Cohort study Prospective	**All**	5.3%	42 cases of malformations, 26 considered severe

(102)	**Huang *et al.* 1999, China**	Placebo-controlled randomized trial (amino acid)	**Chinese herbal medicine**	Not applicable	No abnormal laboratory studies were observed after use of test drug. No obvious allergic reactions were detected.
(85)	**Jafari-Dehkordi *et al.*, 2017, Iran**	Positive-control randomized trial (Vitamin B6)	**Quince**	Not applicable	No adverse events were reported for quince
(60)	**Kalati *et al.*, 2018, Iran**	Placebo controlled triple-blind randomized trial	**Evening primrose oil**	Not applicable	No adverse events were diagnosed in case and placebo groups
#	**Reference**	**Study type**	**Herbal medicinal product**	**Incidence**	**Nature**
(61)	**Kalava *et al.*, 2013, USA**	Placebo-controlled double-blind randomized trial	**Ginger**	12.0%	7% heartburn, 4% diarrhea, 1% mouth irritation
(86)	**Ketsuwan *et al.*, 2018, Thailand**	Placebo-controlled double-blind randomized trial	**Polyherbal hot compress**	0.8%	Skin irritation self-resolved after 24 h
(103)	**Kohama and Inoue, 2006, Japan**	Positive-control open-label trial	**Pine bark**		No adverse events were reported
(75)	**Kolding *et al.*, 2015, Denmark**	Cohort study Prospective	**St. John's wort**	8.1%	Hypospadias, bilateral hip dislocation, heart septum defect
(106)	**Mabina *et al.*, 1997**	Cross-sectional survey	**Isihlambezo**	55.6%	Meconium stained fluid II or III (fetal distress). 55.6% in herbal users vs. 15% in non-users (p = 0.0001)
(120)	**Mann and Zhang, 2014, USA**	Case study	**Polyherbal infusion for milk production and Chinese Herbal Medicine**	Not applicable	No adverse events were observed

(34)	**Nordeng *et al.*, 2011, Norway**	Cross-sectional survey	**Iron-rich herbs**	Not applicable	Mean birth weight was significantly higher in iron-rich herbal users (3793 g vs. 3550 g, p = 0.005) compared to non-users
			Raspberry leaf	Not applicable	Use of raspberry leaf was associated with Cesarean birth (23.5% vs. 9.1%, adjusted OR = 3.47, 95% CI 1.45 - 8.28)
(104)	**Ozalkaya *et al.*, 2018, Turkey**	Placebo controlled randomized trial	**Polyherbal infusion**	Not applicable	"None of the participants complained about adverse events related to tea."
#	**Reference**	**Study type**	**Herbal medicinal product**	**Incidence**	**Nature**
(111)	**Ozturk and Kalayci, 2018, Turkey**	Case reports	***Passiflora incarnata***	Not applicable	Meconium stained amniotic fluid, premature rupture of membranes, meconium aspiration syndrome and pulmonary hypertension of newborn
(77)	**Plaggner *et al.*, 2005, Switzerland**	Cohort study Retrospective	***Bryophyllum pinnatum***	Not applicable	Less adverse drug reactions with *B. pinnatum* alone (group 1) compared to *B. pinnatum* with beta-agonist (Fenoterol, Group 2) (34.3 versus 55.2%, p = 0.02 overall; palpitation, p < 0.5; dyspnea, p = 0.01). More women in Group 2 required additional antibiotics and behtametasone (p < 0.001) compared to Group 1. Less respiratory distress syndrome in Group 1 compared to Group 2 (4.5 versus 19.4%, p = 0.01)
(87)	**Pongrojpaw *et al.*, 2007, Thailand**	Positive-control trial (Dimenhydrinate)	**Ginger**	21.1%	5.9% drowsiness, 15.2% heartburn
(96)	**Portnoi et al., 2003, Canada**	Cohort study Prospective	**Ginger**	1.6%	Ventricular septal defect, right lung abnormality, pelviectasis

(78)	**Räikkönen *et al.*, 2009, Finland**	Cohort study Prospective	**Licorice**	Not applicable	Odds of somatic complaints (AOR 2.35, 95% CI 1.13, 4.9), attention problems (AOR 3.43, 95% CI 1.54, 7.62), rule-breaking behavior (AOR 2.15, 95% CI 1.02, 4.52), aggressive behavior (AOR 2.74, 95% CI 1.20, 6.25), externalizing symptoms (AOR 2.23, 95% CI 1.05, 4.73), somatic problems (AOR 2.48. 95% CI 1.11, 5.55), and ADHD (AOR 2.26, 95% CI 1.04, 4.91) in children aged 8.1 years whose mothers were heavy licorice consumers during pregnancy
#	**Reference**	**Study type**	**Herbal medicinal product**	**Incidence**	**Nature**
(79)	**Räikkönen *et al.*, 2017, Finland**	Cohort study Prospective	**Licorice**	Not applicable	Heavy licorice consumption during pregnancy was associated with: 1. Increase in mean weight ($p<0.001$), increased pubic hair (OR 4.2, 95% CI 1.7, 9.9) and breast development (OR 2.1, 95% CI 1.1, 4.1), and increased Pubertal Development score (OR 5.5, 95% CI 2.4, 12.8) of 12-year-old girl offspring. 2. Significant decrease in mean height ($p=0.031$) of 12-year-old boy offspring; 3. Significantly lower mean general and verbal IQ test scores ($p=0.003$ and $p=0.002$, respectively); and 4. Increased odds of ADHD problems (OR 3.3, 95% CI1.4, 7.7)
(119)	**Roulet *et al.*, 1988, Switzerland**	Case report	**Herbal tea**	Not applicable	Neonatal death due to veno-occlusive disease with hepatic fibrosis by senecionine contamination
(105)	**Rukh *et al.*, 2016, Pakistan**	Positive-control trial (Vitamin B6)	**Ginger**	8.6%	Dry mouth, bloating, sweating. Mild, self-resolved
(62)	**Sadi *et al*., 2016, Iran**	Placebo-controlled double-blind randomized trial	**Saffron**	Not applicable	No adverse events were reported

(63)	**Shahrahmani *et al.*, 2018, Iran**	Placebo-controlled double-blind randomized trial	**Green tea ointment**	Not applicable	No adverse events, infection or sensitivity to ointment were reported by green tea treatment group
(41)	**Shamshirsaz *et al.*, 2009, USA**	Case report	**Ayurvedic medicines**	Not applicable	Lead poisoning, hepatotoxicity, severe
(116)	**Silva *et al.*, 2017, Portugal**	Case report	**Chamomile**	Not applicable	Breast tenderness, engorged breasts
(64)	**Simpson *et al.*, 2001, Australia**	Placebo-controlled randomized trial	**Raspberry leaf**	32.3%	9.4% diarrhea, 4.2% constipation, 8.3% nausea, 4.2% vomiting, 1% headache, 1% heartburn, 2.1% uterine tightening, 1% dizziness, 1% bloating
#	**Reference**	**Study type**	**Herbal medicinal product**	**Incidence**	**Nature**
(88)	**Smith *et al.*, 2004, Australia**	Positive-control randomized trial	**Ginger**	65%	52% dry retching after swallowing, 2% vomiting after ingestion, 2% burning sensation, 9% belching. Belching was significantly ($p < 0.05$) more frequent in ginger group
(121)	**Sridharan, 2009, United Kingdom**	Case report	**Chamomile**	Not applicable	Fetal ductus arteriosus constriction, fetal tachycardia
(112)	**Stavropoulos *et al.*, 2018**	Case report	**Mumijo**	Not applicable	Licorice-like syndrome, pseudo-hyperaldosteronism
(97)	**Strandberg *et al.*, 2001, Finland**	Cohort study Retrospective	**Licorice**	Not applicable	Smaller gestational age was associated with a high intake (≥500 mg/week) of glycyrrhizin (AOR 2.5; 95% CI 1.1, 5.5; $p = 0.03$)
(98)	**Strandberg et al., 2002, Finland**	Cohort study Retrospective	**Licorice**	Not applicable	Increased odds of preterm birth (AOR 2.15; 95% CI 0.93, 4.95) and early preterm birth (AOR 3.07; 95% CI 1.17, 8.05)
(40)	**Tait *et al.*, 2002, South Australia**	Case report	**Ayurvedic medicines**	Not applicable	Chronic lead poisoning, severe hepatotoxicity
(99)	**Trabace *et al.* 2015, Italy**	Cohort study Retrospective	**Melissa, psyllium (polyherbal)**	0.2%	Worsening of stomach ache

			Chamomile	Not applicable	Daily use throughout pregnancy was associated with higher odds of preterm delivery (38.8 ± 1.8 weeks vs. 39.2 ± 1.6 weeks, p < 0.002), increased odds of low birth weight (3230.4 ± 498.6 g vs. 3322.4 ± 511.2 g, p < 0.02), and smaller newborns (49.6 ± 0.9 cm vs. 49.9 ± 1.6 cm, p < 0.05) compared to non-users
			Fennel	Not applicable	Regular use throughout pregnancy was associated with shorter gestational age (38.8 ± 2.2 weeks vs. 39.1 ± 1.6 weeks, p < 0.05) compared to non-users
			Ginger	Not applicable	Regular use was associated with a shorter gestational age (38 ± 3.3 weeks vs. 39.1 ± 1.7 weeks, p < 0.05) and smaller newborn head circumference (32.1 ± 3.5 cm vs. 34.2 ± 1.8 cm, p < 0.002) compared to non-users
#	**Reference**	**Study type**	**Herbal medicinal product**	**Incidence**	**Nature**
(65)	**Tabeshpour *et al.*, 2017, Iran**	Placebo-controlled double-blind randomized trial	**Saffron**	17.9%	Bleeding gums (2.6%), gastrointestinal disorder (5.1%), oversleeping (2.6%), lack of sleep (2.6%), and low breast milk supply (5.1%)
(113)	**Thomas and Jones, 1998, USA**	Case report	**Blue cohosh**	Not applicable	Neonatal anterolateral myocardial infarction, cardiogenic shock and congestive heart failure
(66)	**Tianthong and Phupong, 2018, Thailand**	Placebo-controlled double-blind randomized trial	**Ginger**	33.7%	Constipation, nausea, vomiting, diarrhea, heartburn, others
(67)	**Vutyavanich *et al.*, 2001, Thailand**	Placebo-controlled double-blind randomized trial	**Ginger**	28.1%	18.8% headache, 3.1% abdominal discomfort, 3.1% heartburn, 3.1% diarrhea. Minor.
(68)	**Wagner *et al.*, 2018, U.S.A.**	Placebo-controlled double-blind randomized trial	**Polyherbal infusion for milk production**	5.9%	Digestive, respiratory, dermatological, breast and other symptoms

(89)	**Willetts *et al.*, 2003, Australia**	Placebo-controlled double-blind randomized trial	**Ginger**	15.1%	6.7% reflux and heartburn, 1.7% allergic reaction, 1.7% dehydration, all severe enough to withdraw. 5% spontaneous abortion
(39)	**Wong *et al.*, 2015, Australia, UK**	Case report	**Ayurvedic medication**	Not applicable	Lead poisoning. **In mother:** normocytic anemia, lethargy, oligohydramnios, IUGR. **In fetus:** absence of the right kidney, small echogenic left kidney with poor cortical-medullary differentiation, died at 2 days of life from severe respiratory failure due to underdeveloped lungs because of severe renal dysgenesis
(69)	**Yuan *et al.*, 2016, China**	Placebo-controlled double-blind randomized trial	**Capsaicin-containing chili**	70.0%	10% diarrhea, 20% heat sensation in mouth, 10% skin wheals, 30% increased frequency of defecation. Mild to moderate, self-resolved.
#	**Reference**	**Study type**	**Herbal medicinal product**	**Incidence**	**Nature**
(100)	**Zamawe *et al.*, 2018, U.K.**	Cohort study Retrospective	**Mwanamphepo**	25.7%	Increased odds of maternal morbidity among users compared to non-users of Mwanamphepo (AOR = 1.28; 95% CI = 1.09–1.50), increased odds of neonatal death or morbidity (AOR =1.22; 95% CI = 1.06–1.40) among neonates whose mothers used Mwanamphepo compared to non-users
(117)	**Zengin *et al.*, 2015, Turkey**	Case report	**Fennel and cumin**	3 cases	Acute hepatitis: nausea, vomiting, anorexia, weakness, abdominal discomfort, elevated liver enzymes and bilirubins

Appendix 4. Herb-Drug Interactions During Pregnancy and the Postnatal Period

#	Reference	Study type	Herbal medicinal product	Incidence	Nature
(110)	**Cheang *et al.,* 2016, USA**	Case report	**Raspberry leaf**	Not reported	Insulin and raspberry leaf, moderate, causing hypoglycemia
(14)	**Holst *et al.,* 2008, Norway**	Cohort study Prospective	**All**	Not reported	Multivitamins, folic acid, antihypertensive drugs, NSAIDs, analgesics and psycholeptics
(76)	**McLay et al., 2017, United Kingdom**	Cross-sectional survey	**All**	12.7% (3.05% minor, 93.9% moderate, 3.05% major)	Aloe and insulin; chamomile and diazepam, propranolol, diclofenac, ondansetron (minor), chloropromazine, dyhidrocodeine, co-comadol; cranberry and diazepam, diclofenac; ginger and metformin, insulin, aspirin, nifedipine (potentially major); ginseng and metformin, diazepam; grapefruit and itraconazole, propranolol, diclofenac, omeprazole; sage and co-comadol
(31)	**Moussally *et al.,* 2009, Canada**	Cohort study Prospective	**All**	38.4%	9.3% potentially serious, 9.4% could affect drug metabolism, 19% of used herbs could bind with all drugs, 0.7% hepatotoxic combinations
(34)	**Nordeng et al., 2011, Norway**	Cross-sectional survey	**All**	2.50%	1.3% ginger and acid suppressant, 0.67% chamomile and psychotropic drugs, 0.33% iron-rich herbs and acid suppressants, 0.17% dandelion and furosemide

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