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Overview of Contraindicated Chinese Medicines for Pregnancy

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Additional information is available at the end of the chapter

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Abstract

Chinese medicines should be classified into drugs, which have both beneficial and harmful effects. For centuries, Chinese medicines have been widely used to relieve many symptoms and to treat complications during pregnancy. It is not clear how safe the Chinese medicines are being used during pregnancy and if there is any adverse effects to embryofetal development and prenatal and postnatal growth. Some Chinese medicines are indicated that they cannot be used in pregnancy. In this chapter, we will conduct a systematic review to summarize and characterize in details the Chinese medicines classified as contraindicated, not recommended and cautiously used for pregnancy in most updated version of Pharmacopeia of the People's Republic of China. Clinical reports including clinical trials, case reports, case series and animal studies including short-term and long-term toxicity, specific organ toxicity and different species of the Chinese medicines will be studied. Unlike those pharmaceutical drugs not recommend for use during pregnancy because of known or suspected adverse or teratogenic effects evident by animal studies and/or clinical trials, most of the Chinese medicines were utilized for long history in culture which, however, has very limited scientific data regarding the adverse pregnant outcomes.

Keywords: Chinese medicines, pregnancy, safety, review

1. Introduction

1.1. Chinese medicines for pregnancy

1.1.1. Application in China

Chinese medicines have become very popular and are widely applied to different kinds of medical conditions during pregnancy [1]. It promotes both mothers' and fetuses' health,

relieves and cures common disorders in women [1]. It has been used as a main stream medicine in China with a longer history than Western medicines.

The first record of Chinese medicines treatment related to reproductive was first explained in A Chinese Bestiary 3000 years ago during Xia, Shang and Zhou era [2, 3]. Since then, Gu Rong was commonly used for contraception [2, 3]. In the following centuries, considerable progress was achieved in both clinical theory and practice while lots of milestones have been developed in Obstetrics and Gynecology. Due to historical factors of the late Qing Dynasty, and the influence of Western Medicine under the Renaissance, development of Chinese Medicine was less prominent [4]. After the establishment of People's Republic of China, with the great efforts of lots of Chinese Medicine practitioners and researchers, 6th edition of the textbook "Traditional Chinese Medicine in Obstetrics and Gynecology" [4] and lots of reference books and monographs have been published and used for daily teaching, training and self-learning. Apart from medical educations in Chinese Medicine, researches in collaborations with Chinese medicines and Western medicines have been raised to a new level and lots of meaningful conclusions have been drawn. For example, it was reported that combined Chinese medicines and Western medicines for ectopic pregnancy were more effective than conventional treatment [5, 6], and the method of combined medicines has been well studied and applied widely since then.

1.1.2. Development in foreign countries

Chinese Medicine in China has a long history, but its development for pregnant women in other countries is just within recent centuries. In foreign nations, the most common treatments are Acupuncture and Chinese herbal medicines (CHMs). Other therapies of Chinese Medicine, which could be used during pregnancy, began to spread to the world in very late twentieth century, such as Tui Na Massage and Die Da [4].

Chinese herbal medicines (CHMs) spread to the world earlier than acupuncture but only widely applied lately, due to the early advancement and modernization of Western medicines in foreign countries [7]. For instance, the "European Pharmacopoeia" had been locally well-developed, and Chinese herbs as medicines were not attractive to the practitioners and patients. With the advantages of Chinese medicines, including less side effects and greater effectiveness in some chronic diseases (such as infertility and irregular menstruation) than Western medicines, it was gradually accepted by foreigners and now has been spread to over 160 countries [3]. More and more foreign researchers and clinical doctors seriously have interests in it and come to China for further study.

1.1.3. Effectiveness and efficacy

With a long history of application of Chinese medicines to treat pregnant disorders, large amounts of case reports and clinical trials have been reported [8]. However, until now, limited data are available to overview Chinese medicines for pregnancy. Our team has reported in a systematic review [9] about the general applications, including common formulae, common individual CHMs, dosage and dosing, frequency, therapeutic efficacy, clinical indications and so on.

Chinese medicines are prescribed in formulae, and the Chinese medicine practitioners decide the formula according to the clinical presentation. Based on medical knowledge and personal experience, some use original or traditional formula, the others have individual prescription as personalized medicine. The prescribed formulae vary a lot, some formulae even lack unified theory and scientific evidence. Therefore, under a long-term collaboration with Cochrane Review Pregnancy and Childbirth Group, our team has conducted two systematic reviews with meta-analyses to study the claimed efficacy of Chinese herbal medicines for pregnancy-related disorders [10, 11]. The results showed that combined Chinese herbal medicines and other pharmaceuticals are more beneficial than other pharmaceuticals alone for threatened miscarriage [10] and unexplained recurrent miscarriage [11], but the evidence on the effectiveness and safety of Chinese herbal medicines alone as treatment is still insufficient, due to the poor qualities of the included clinical trials.

1.1.4. Safety

Safety is always the biggest issue in daily medical practice, and the issue is also a major concern to pregnant women. Chinese herbal medicines have been used to treat diseases and complications during pregnancy, and it is apparently well accepted as with fewer side effects.

There are 31 Chinese herbal medicines that were classified as toxic and contraindicated during pregnancy, which have been listed in many textbooks. The website of Chinese Medicine Council of Hong Kong (CMCHK) recently released another five CHMs, which contain aristolochic acid, which could induce abortion, kidney damage and cancer. Further studies of these Chinese herbal medicines have been carried out in the last 20 years and have demonstrated their adverse effects on both/either mothers and/or newborns. For example, Kansui Root (*Radix Kansui*, *Gan Sui*) is prohibited in pregnancy because it can poison the fetus and stimulate uterine contraction [12].

On the other hand, numbers of clinical trials have also been carried out to assess the safety of some Chinese herbal medicines in pregnancy and associated conditions, or to compare the adverse effects of Chinese herbal medicines with other medicines. Among the commonly used Chinese medicines, there are not too many studies of their potential harmful effects however. Our team has carried out a systematic review [13, 14] with meta-analyses to record the potential adverse effects and safety issues of CHMs as treatment for threatened miscarriage, but conclusive results remain elusive, as studies varied considerably in design, interventions and outcome measures. In the absence of placebo-controlled trials, the safety of Chinese medicines for the treatment of threatened miscarriage is unknown. Rigorous scientific and clinical studies to assess the possible risks of Chinese medicines are needed.

In conclusion, it is not clear how safe the Chinese medicines are being used during pregnancy and if there is any adverse effects to embryo-fetal development and prenatal and postnatal growth.

1.2. Chinese pharmacopeia

Unlike those pharmaceutical drugs not recommend for use during pregnancy because of known or suspected adverse or teratogenic effects evident by animal studies and/or clinical

trials, most of the Chinese medicines were utilized for long history in culture which, however, has very limited scientific data regarding the adverse pregnant outcomes.

“Chinese Pharmacopeia”, acknowledged by World Health Organization (WHO) as the official pharmacopeia for Chinese medicines, records 1146 different Chinese medicines [15]. It provides information on the herbs with their characteristics, identity, impurity, contents, extractum, analysis, property and channel, therapeutic action, pharmacological data, dose and dosing, precautions, storage, authentication methods and so on.

Among all this valuable information, we will obtain the most specific safety information for pregnancy from the Chinese Pharmacopeia and provide to the doctors, scholars and patients as scientific evidence on the safe application of Chinese medicines during pregnancy.

2. Objective

In this chapter, we will conduct a systematic review to summarize and characterize in details the Chinese medicines classified as contraindicated, not recommended and cautiously used for pregnancy in the most updated version of Chinese Pharmacopeia. Clinical reports including clinical trials, case series, case reports and animal studies including short-term and long-term toxicity, specific organ toxicity and different species of Chinese medicines will be studied.

3. Method

3.1. Search in Chinese pharmacopeia

Two review assessors carried out the word-by-word study in Chinese Pharmacopeia to identify the study medicines. First, they read all the recorded individual Chinese medicines and the formulae one by one and recorded in a list of the medicines remarked with application in pregnancy. Second, they checked the details of pharmaceutical effects and clinical functions and indications of these list-out medicines. If any adverse effects related to pregnancy were reported, the reference study would be traced and more details of the adverse outcomes were recorded, for further summaries and analyses. Third, they carried out the same rules to expand the search in different online databases, if the details of the adverse outcomes could not be accessed from the Chinese Pharmacopeia or the reference study. Finally, they extracted and summarized the specific safety information on three classifications of these Chinese medicines.

3.2. Search in other databases

To further supplement the pharmacological and toxicology data of the Chinese medicines, several online national and public resources on World Wide Web were also referred. It included Center for Food Safety and Applied Nutrition (CFSAN) from US Food and Drug Administration (FDA, (<http://vm.cfsan.fda.gov/~dms/supplmnt.html>), National Center

for Complementary and Alternative Medicine (NCCAM) from US National Institute of Health (NIH, <http://nccam.nih.gov>), Agricultural Research Service (ARS) from US Department of Agriculture (USDA, <http://www.ars-grin.gov/duke>), Medical Dictionary for Regulatory Activities (MedDRA) from International Federation of Pharmaceutical Manufacturers and Associations (IFPMA, <http://www.meddrasso.com>), National Council Against Health Fraud (NCAHF) from a private health agency (<http://www.ncahf.org>), Quackwatch from an American non-profit organization (<http://www.quackwatch.com>), HerbMed from Alternative Medicine Foundation (<http://www.herbmed.org>) and ConsumerLab from an independent laboratory (<http://www.consumerlab.com>), accessibility verified until 1 September 2016.

3.2.1. Search strategies for online databases

Search by subject heading/keyword/abstract/full text with:

1. Traditional Chinese medicines
2. Pregnancy
3. Western medicines
4. Comparisons studies
5. Safety
6. Toxicity

Or could be included or replaced by similar words:

1. Herbal medicines
2. Pharmaceuticals
3. Obstetric disorders
4. Pregnancy diseases
5. Therapy

Only clinical trials, which assessed the adverse pregnant outcomes of the Chinese medicines, were further selected for meta-analysis.

3.3. Study criteria

3.3.1. Types of studies

All published studies (list in Chinese Pharmacopeia and reference and reference of reference) that evaluated the safety of Chinese medicines for pregnancy were included. Studies of Chinese medicines for other clinical applications and in animal, chemical and basic research were included. (Non)/Randomized control trials, case controlled studies, case series, case reports, commentary articles and non-systematic reviews were excluded. Studies with no evaluation or incomplete records of adverse pregnancy outcome were also included.

Language of the publications was restricted to English and Chinese. Literature with either English or Chinese abstract should be available for initial search. No translation was required for Chinese articles as all review assessors can read Chinese and understand Traditional Chinese Medicine and Chinese medicines thoroughly. Translations were only sought from the language facilities of the university for articles written in English and Chinese.

3.3.2. *Types of participants*

There was no strict for types of participants, as we collected all safety information then further extracted for the summary table (**Table 1**).

3.3.3. *Types of interventions*

Since Chinese medicines are crude drugs of plant, animal and mineral origins, not only those Chinese medicines originated from plants or herbs but also those from animals and minerals were included. All types of Chinese medicine in either standard or combined formulas used during pregnancy or on pregnancy model animals regardless of the dose or duration of administration.

3.3.4. *Types of outcome measures*

General and specific adverse effects of the study Chinese medicines were recorded. Adverse reproductive outcomes in both mothers and fetuses/infants (both human and animals) will be recorded. Maternal outcomes included (1) toxicity (e.g. renal failure, liver failure, neurological impairment and death); (2) side-effects (e.g. anaphylaxis, gastrointestinal disturbance, hypertension/hypotension, cardiac arrhythmia, gestational diabetes and so on); (3) pregnancy loss (e.g. late abortion, intrauterine death and still birth) and (4) pregnancy complications (e.g. preterm/postdate labor, placenta previa, placenta abruption and so on). Fetal outcomes included (5) perinatal mortality (including prenatal and postnatal death); (6) toxicity (e.g. fetal compromise, neurological consequences, hydrops fetalis and so on); (7) congenital malformations and (8) neonatal complications (e.g. jaundice, infection, hypoglycemia and so on). Both long- and short-term adverse outcomes were reported and summarized.

3.3.5. *Data collection and analysis*

For each reference study to be involved in this review, all review assessors first screened the titles, abstract sections and keywords of every record to exclude the duplicates and obvious false positive. Second, full text of eligible studies was assessed for further inclusion or exclusion. If there was sufficient information and it met the inclusion criteria, the study was included in the analyses and summaries. Two review assessors assessed the studies for inclusion independently; any disagreement was resolved by discussion among all the review authors. The study authors were contacted for clarification if there were doubts about the eligibility of the study and the disagreement could not be resolved. The review authors were not blinded to the journal of origin or institution.

	CHM (English)	CHM (Biological name)	CHM (Chinese)	Dose	Actions and clinical indications	Classification in pregnancy
1	Aconiti kusnezoffii radix	Aconitum kusnezoffii Reichb.	草乌 (Cao Wu)	After preparation	To restore yang, to improve fire, and to disperse cold. Being used in: sweating profusely with body temperature dropping; muscle spasm in cholera; instant sweating, afraid of cold in cases of yangxu (yang deficient); pain and cold in chest and abdomen, chronic diarrhea due to pixu (spleen deficient), chronic muscle or joint pain due to wind cold dampness, tightness and pain in joints and muscles; edema and coldness in the lower legs due to shenyangxu (kidney yang deficient)	Contraindicated
2	Aconiti radix	Aconitum carmichaelii Debx.	川乌 (Chuan Wu)	After preparation	To restore yang, to improve fire, and to disperse cold. Being used in: sweating profusely with body temperature dropping; muscle spasm in cholera; instant sweating, afraid of cold in cases of yangxu (yang deficient); pain and cold in chest and abdomen, chronic diarrhea due to pixu (spleen deficient), chronic muscle or joint pain due to wind cold dampness, tightness and pain in joints and muscles; edema and coldness in the lower legs due to shenyangxu (kidney yang deficient)	Contraindicated
3	Anemones raddeanae rhizoma	Anemone raddeana Regel	两头尖 (Liang Toujian)	1-3	Rheumatism	Contraindicated
4	Aristolochiae fructus	Aristolochia debilis Sieb.et Zucc	马兜铃 (Ma Douling)	3-9	In coughs, phlegm, wheezing, blood in phlegm, with lung heat; hypertension, dizziness, with red face due to yinxu and liver yang ascending (gan yang ascending) condition; bleeding hemorrhoids and swelling in the anus	Contraindicated
5	Aristolochiae herba	Aristolochia debilis Sieb.et Zucc; Aristolochia contorta Bge.	天仙藤 (Tian Xianteng)	3-6	Same as 4	Contraindicated
6	Calomel	Calomelas	轻粉 (Qing Fen)	0.1-0.2	Use externally to kill parasites; for ringworms, boils and syphilis. Take internally to promote urination and bowel movements. Usually use with other water-removing herbs in difficulty in urination and defecation	Contraindicated
7	Cinnabaris	Mercury sulfide	朱砂 (Zhu Sha)	0.1-0.5	Insomnia	Contraindicated

	CHM (English)	CHM (Biological name)	CHM (Chinese)	Dose	Actions and clinical indications	Classification in pregnancy
8	Crotonis fructus	Croton tiglium L.	巴豆 (Ba Dou)	Proper dose	As laxative for constipation, distention, abdominal fullness and pain, caused by extreme coldness of bowels; for ascites; for clogged phlegm; for topical uses for abscesses and ulcers, to speed up ulceration of abscesses	Contraindicated
9	Crotonis semen pulveratum	Croton tiglium L.	巴豆霜 (Ba Doushaung)	0.1–0.3	Same as 8	Contraindicated
10	Curcumae rhizoma	Curcuma phaeocaulis Val.	莪术 (E Zhu)	6–9	Promotes qi flow and rids of blood stasis, amenorrhea due to blood stasis; distension and pain due to stagnation of undigested food; early stages of cancer in the cervix uteri (neck of uterus)	Contraindicated
11	Daturae flos	Datura metel L.	洋金花 (Yang Jinhua)	0.3–0.6	The flowers are being used in anesthesia, as sedative and for inducing sleep. The leaves are being used in rheumatoid arthritis. The seeds are being used in promoting blood circulation and in ridding of pain	Contraindicated
12	Erycibe schmidtii	Erycibe obtusifolia Benth.	丁公藤 (Ding Gongteng)	3–6	Rheumatism	Contraindicated
13	Euphorbiae pekinensis radix	Euphorbia pekinensis Rupr.	京大戟 (Jing Daji)	1.5–3	For edema, ascites, retention of phlegm, tuberculosis of lymph nodes. Can be taken internally or applied externally	Contraindicated
14	Euphorbiae semen	Euphorbia lathyris L.	千金子 (Qian Jinzi)	1–2	Dermatomycosis	Contraindicated
15	Euphorbiae semen pulveratum	Euphorbia lathyris L.	千金子霜 (Qian Jinzishaung)	0.5–1	Dermatomycosis	Contraindicated
16	Eupolyphaga steleophaga	Eupolyphaga sinensis Walker	土鳖虫 (Tu Biechong)	3–10	For blood stasis, amenorrhea, injuries of bones and muscles from impact, sprain in loin area	Contraindicated
17	Ferulae resina	Ferula sinkiangensis K.M. Shen; Ferula fukanensis K.M. Shen	阿魏 (A Wei)	1–1.5	Being used in ridding of parasites, improving meat digesting, treating purpura, epilepsy, enlarged liver	Contraindicated
18	Genkwa flos	Daphne genkwa Sieb. et Zucc.	芫花 (Yuan Hua)	1.5–3	For edema, ascites. For worm parasite: vinegar processed yuan hua, xiong huang. Make into powder. Take internally. For head fungal or ringworm: mix with lard and apply topically	Contraindicated

	CHM (English)	CHM (Biological name)	CHM (Chinese)	Dose	Actions and clinical indications	Classification in pregnancy
19	Gleditsiae fructus abnormalis	Gleditsia sinensis Lam.	猪牙皂 (Zhu Yazao)	1–1.5	Oral: for sequelae of strokes, losing consciousness, epilepsy with abundance of phlegm, difficulty in expelling phlegm, constipation. External usage: boils; breast engorgement in new mothers: wrap a peanut size powdered zhu ya zao in clean gauze. Dip it in 75% alcohol to wet the outer layer. Stuff it in the nostril (same side as the engorgement is) for 12 hours. If necessary repeat treatment after rested for 8 hours	Contraindicated
20	Ground beetle	Eupolyphaga sinensis Walker	虻虫 (Zhe Chong)	3–10	For blood stasis, amenorrhea, injuries of bones and muscles from impact, sprain in loin area	Contraindicated
21	Hirudo	Hirudo nipponica Whitman	水蛭 (Shui Zhi)	1–3	For treatment of blood stasis, asthma, amenorrhea, physical injuries, unable to conceive, also used in abortion. Live shui zhi used externally in treating tumors, rid of swelling in boils, local blood clots (bruises)	Contraindicated
22	Hydrargyri oxydum rubrum	Hydrargyri Oxydum Rubrum	红粉 (Hong Fen)	Proper dose	Suppurative infection	Contraindicated
23	Hyoscyami semen	Hyoscyamus niger L.	天仙子 (Tian Xianzi)	0.06–0.6	Relieving spasm	Contraindicated
24	Kansui radix	Euphorbia kansui T.N. Liou ex T.P. Wang	甘遂 (Gan Sui)	0.5–1.5	Anti-inflammation	Contraindicated
25	Moschus	Moschus berezovskii Flerov	麝香 (She Xiang)	0.03–0.1	For coma due to stroke, angina, tumors and carbuncles, hastens delivery and facilitate the passage of stillborns. Seizures	Contraindicated
26	Mylabris	Mylabris phalerata Pallas	斑蝥 (Ban Mao)	0.03–0.06	For cancer, skin fungus infection, cancer of the lymphatic system, boils cannot ripen, dead tissues	Contraindicated
27	Nigellae semen	Nigella glandulifera Freyn et Sint.	黑种草子 (Hei Zhongcaozi)	2–6	For treatment of: heart palpitation, insomnia, weakness, cold or flu, cough	Contraindicated
28	Papaveris pericarpium	Papaver somniferum L.	罂粟壳 (Ying Suke)	3–6	Pain relief	Contraindicated
29	Pharbitidis semen	Pharbitis nil (L.) Choisy; Pharbitis purpurea (L.)Voigt	牵牛子 (Qian Niuzi)	3–6	Edema; ascites; constipation; difficulty in urination; beri beri; flatulence; abundance of phlegm, cough, asthma; abdomen pain with parasite	Contraindicated

	CHM (English)	CHM (Biological name)	CHM (Chinese)	Dose	Actions and clinical indications	Classification in pregnancy
30	Phytolaccae radix	Phytolacca acinosa Roxb.	商陆 (Shuang Lu)	3–9	Promote diuresis	Contraindicated
31	Realgar	Realgar	雄黄 (Xiong Huang)	0.05–0.1	Topical application for ridding of parasites: for scabies, ringworm, damp rashes, abscesses, ulcerations, snake bites. Taking internally for intestinal parasites, especially effective for roundworms. Dries dampness: expels phlegm	Contraindicated
32	Rhododendri mollis flos	Rhododendron molle G. Don	闹羊花 (Nao Yanghua)	0.6–1.5	Alleviates pain. Being used in rheumatoid arthritis, pain in broken bones, fungal infection of the skin	Contraindicated
33	Scolopendra	Scolopendra subspinipes mutilans L. Koch	蜈蚣 (Wu Gong)	3–5	Epilepsy, spasm, scrofula, sores, arthritis, hemorrhoid with pain, snake poison, scalding, leukemia, stroke	Contraindicated
34	Scorpio	Buthus martensii Karsch	全蝎 (Quan Xie)	0.6–9	Epilepsy, stroke, paralysis, migraine, pain in arthritis, tetanus, tuberculosis in lymph nodes, urticaria, and bunacles	Contraindicated
35	Sparganii rhizoma	Sparganium stoloniferum Buch.-Ham.	三棱 (San Leng)	5–10	Painful menses. Postpartum complication, amenorrhea cause by qi stagnation and/or blood stasis. Cu san leng (prepared with vinegar) is stronger in pain inhibition. Fu san leng (stir fried with flour) is milder and is being used in promoting digestion	Contraindicated
36	Strychni semen	Strychnos nux-vomica L.	马钱子 (Ma Qianzi)	0.3–0.6	Rheumatoid arthritis, injuries, boils and swellings, sequelae from polio of children, impotence, for diseases of the gastrointestinal tract, organic and functional disorders of the heart and circulatory system, glycine encephalopathy, nervous conditions, myasthenia gravis; amyotrophic lateral sclerosis (als), cancer, depression, migraine, menopausal syndromes, facial neuralgias, raynaud's syndromes	Contraindicated
37	Strychni semen pulveratum	Strychnos nux-vomica L.	马钱子粉 (Ma Qianzifen)	0.3–0.7	Same as 36	Contraindicated
38	Toxicodendri resina	Toxicodendron vernicifluum (Stokes) F.A. Barkl	干漆 (Gan Qi)	2–5	Elimination of parasite	Contraindicated
39	Gleditsiae sinensis fructus	Moschus berezovskii Flerov	大皂角 (Da Zaojiao)	1–1.5	1. Dispels phlegm or coughs with abundance of phlegm; 2. Opens the orifices after strokes or epilepsies or facial paralysis due to excessive of phlegm; 3. Discharges puss when used externally for boils. Zao jiao ci uses: early stages of boils, difficulty in discharging of pus, eczema, and leprosy	Not recommended

	CHM (English)	CHM (Biological name)	CHM (Chinese)	Dose	Actions and clinical indications	Classification in pregnancy
40	Saussureae involucratae herba	Saussurea involucrata (Kar. et Kir.) Sch.-Bip.	天山雪莲 (Tian Shanxuelian)	3–6	For hardening of blood vessels of the brain, tumor. Folk applications include rheumatoid arthritis, impotence, irregular menses, placenta not being expelled after birth	Not recommended
41	Abelmoschi corolla	Abelmoschus manihot (L.) Medic.	黄蜀葵花 (Huang Shuhuaihua)	3–30	Promote diuresis	Cautiously used
42	Achyranthis bidentatae radix	Achyranthes bidentata Bl.	牛膝 (Niu Xi)	5–12	Damp cold, weakness and pain in loin and knees, tight and spastic limbs, irregular menses, postpartum pain in abdomen due to blood stasis, afterbirth not being expelled, blood in urine, physical injuries and difficulty in bending knees. Raw huai niu xi is effective for breaking blood stasis. Cooked huai niu xi is effective for strengthening muscles and bones, promoting urination and strengthening essence of the body	Cautiously used
43	Aconiti kusnezoffii folium	Aconitum kusnezoffii Reichb.	草乌叶 (Cao Wuye)	1–1.2	Same as 1	Cautiously used
44	Aconiti kusnezoffii radix cocta	Aconitum kusnezoffii Reichb.	制草乌 (Zhi Caowu)	1.5–3	Same as 1	Cautiously used
45	Aconiti lateralis radix praeparata	Aconitum carmichaelii Debx.	附子 (Fu Zi)	3–15	Similar as 2	Cautiously used
46	Aconiti radix cocta	Aconitum carmichaelii Debx.	制川乌 (Zhi Chuanwu)	1.5–3	Same as 2	Cautiously used
47	Aloe	Aloe barbadensis Miller; Aloe ferox Miller	芦荟 (Lu Hui)	2–5	For constipation, dizziness, red eyes, and irritability due to heat buildup (yinxu (yin deficient) with heat). Kills intestinal parasites, especially roundworms. For treatment of ringworms. For burns and wounds. For treatment of liver yang over active	Cautiously used
48	Arisaematis rhizoma	Arisaema erubescens (Wall.) Schott	天南星 (Tian Nanxing)	Proper dose	Being used in stroke with abundance of phlegm, paralysis, epilepsy, tetanus, tumors, arrhythmia. External use: insect and snake bites (grind with vinegar or water and apply to affected area)	Cautiously used

	CHM (English)	CHM (Biological name)	CHM (Chinese)	Dose	Actions and clinical indications	Classification in pregnancy
49	Arisaematis rhizoma preparatum	Arisaeme erubescens (Wall.) Schott	制天南星 (Zhi Tiannanxing)	3-9	Same as 48	Cautiously used
50	Aurantii fructus	Citrus aurantium L.	枳壳 (Zhi Qiao)	3-10	Indigestion due to low function; bloating in chest, abdomen and solar plexus area; constipation; diarrhea but difficult to expel, focal distention; fullness in the chest; cough with abundance of phlegm; prolapse of stomach, uterus and rectum	Cautiously used
51	Aurantii fructus immaturus	Citrus aurantium L.	枳实 (Zhi Shi)	3-10	Same as 50	Cautiously used
52	Borneolum	Cinnamomum camphora (L.) Presl	天然冰片 (Tian Ranbingpian) / 右旋龙脑 (You Xuanlongnao)	0.3-0.9	For fainting due to strokes or heat, bunacle, pain in joints, ulceration of the cornea, sores in the mouth, eczema, taking internally: mainly being used in pills; seldom in decoction. External application: for washing or added in external medication	Cautiously used
53	Borneolum syntheticum	Borneol	冰片 (Bing Pian) / 合成龙脑 (He Chenglongnao)	0.15-0.3	Similar as 58	Cautiously used
54	Bovis calculus	Bos taurus domesticus Gmelin	牛黄 (Niu Huang)	0.15-0.35	Anti-inflammatory, anti-fever, anti-bacterial, opens the orifices, awakens the spirit, rid of phlegm. For high fever with delirium and convulsion due to hot diseases with hot phlegm, for chronic sore throat, for abscesses that have ripen and ruptured. Clears the heart, liver, relieves toxicity, rid of wind and tremors. For convulsions with high fever due to liver heat	Cautiously used
55	Bovis calculus artifactus	Bos taurus domesticus Gmelin	人工牛黄 (Ren Gongniu Huang)	0.15-0.35	Same as 54	Cautiously used
56	Bovis calculus sativus	Bos taurus domesticus Gmelin	体外培育牛黄 (Ti Waipei yuni Huang)	0.15-0.35	Same as 54	Cautiously used

	CHM (English)	CHM (Biological name)	CHM (Chinese)	Dose	Actions and clinical indications	Classification in pregnancy
57	Bufonis venenum	Bufo bufo gargarizans Cantor	蟾酥 (Chan Chu)	0.015–0.03	For food poisoning with stomach pain and bloating, vomiting with diarrhea, even fainting. Usually combine with she xiang, ding xiang, cang zhu, like formula called chan su wan. For bunacles, scofula, painful and swollen throat and various kinds of toothache: combine with xiong huang, ku fan, zhu sha, etc. Make into pills the sizes of mung beans. Take five pills each time with decoction of white portions of green onion. For scarlet fever usually combine with niu huang, xiong huang, bing pian, like liu shen wan. Being used in various types of cancer, like liver cancer, intestine cancer, leukemia, skin cancer, etc. Taking orally or external application has been successful to certain degree, according to some reports. Being used in respiratory and in circulatory exhaustion. It possesses the effect of raising blood pressure for long time. It also possesses respiratory stimulating effect	Cautiously used
58	Camphis flos	Camphis grandiflora (Thunb.) K. Schum.	凌霄花 (Ling Xiaohua)	5–9	Flower: for irregular menses, amenorrhea, tumors of the uterus, ovaries, endometriosis, mammary glands hyperplasia, chronic inflammation of the pelvic area, postpartum breast swelling, rubella, erysipelas, itchy skin, rosacea, acne. Roots: for rheumatoid arthritis, injuries from impact, broken bones, dislocations, acute infection of the digestive tract	Cautiously used
59	Carthami flos	Carthamus tinctorius L.	红花 (Hong Hua)	3–10	Actions and indications: 1. Being used in lumps in intestines and bowels, sores and carbuncles, pain from impact injuries, rheumatoid arthritis, invigorates circulation, breaks up blood stasis condition, and promotes menstruation: injuries from impact, swollen boils, irregular menses, pain in stopping of menses, pain from blood stasis after birth. Small amount can invigorate circulation and large amount can get rid of blood clots. It is an important herb in blood stasis therapy and often is prescribed with tao ren. To invigorate circulation, it is often used with dang gui, chuan xiong, shao yao. To rid of blood stasis, it is used with san leng, e zhu, and da huang; 2. Measles with blood stasis, color not lively red: use hong hua, dang gui, zi cao, da qing ye; 3. Angina of coronary diseases: use hong hua, dan shen, chuan xiong, chi shao; 4. Thromboangitis obliterans: use hong hua, dang gui, tao ren, chi shao, ru xiang; 5. For treatment of enlargement of the liver and spleen; 6. For physical injuries with blood stasis and pain: broken bones, dislocated joints, sprains, and impact	Cautiously used

	CHM (English)	CHM (Biological name)	CHM (Chinese)	Dose	Actions and clinical indications	Classification in pregnancy
***60	Cinnamomi cortex	Cinnamomum cassia Presl	肉桂 (Rui Gui)	1–5	Tonic for stomach, rid of wind, to promote sweating, for headache, anemia, cold limbs, to promote urination. To promote lung qi, in chill and fever, cold phlegm, diarrhea, muscle spasm, headache, back pain, sweating, to stop easily being annoyed, strengthening muscles and bones, promote circulation. Use in impotence due toshenyangxu (kidney yang deficient)	Cautiously used
61	Cinnamomi ramulus	Cinnamomum cassia Presl	桂枝 (Gui Zhi)	3–10	Same as 60	Cautiously used
62	Coicis semen	Coix lacryma-jobi L. var.ma-yuen (Roman.) Stapf	薏苡仁 (Yi Yiren)	9–30	For improving digestion, enhancing the lung function, ridding of bacterial or fungal infection, arresting pain and itchiness. For treatment of spastic muscles, arthritis pain in joints and muscular rigidity. Beri-beri and edema, vagina yeast infection, stones in the urinary tract, neuralgia, difficulty in urination, lung abscess, gonorrhea, restless leg syndrome. Use raw yi yi ren for infection. Use stir fried yi yi ren for improving digestion	Cautiously used
63	Croci stigma	Crocus sativus L.	西红花 (Xi Honghua)	1–3	Similar as 59	Cautiously used
64	Cyathulae radix	Cyathula officinalis Kuan	川牛膝 (Chuan Niuxi)	5–10	Rheumatism, hematuria, amenorrhea, abdominal mass (fibroids of the uterus, ovarian cysts, endometriosis, pelvic inflammation, blood retention due to gynatresia, extra-uterine pregnancy, bleeding in the uterus, and other pelvic masses)	Cautiously used
65	Dianthi herba	Dianthus superbus L.	瞿麦 (Qu Mai)	9–15	Gonorrhea, edema, urinary tract inflammation, difficulty in urination, irregular menses, amenorrhea, dystocia, carbucle	Cautiously used
66	Dichroae radix	Dichroa febrifuga Lour.	常山 (Chang Shan)	5–9	Vomitting, malaria	Cautiously used
67	Echinopsis radix	Echinops latifolius Tausch.; Echinops grijisii Hance	禹州漏芦 (Yu Zhouloulu)	5–10	For boils, carbuncles, acute mastitis, unable to discharge milk	Cautiously used
68	Euphorbiae hirtae herba	Euphorbia hirta L.	飞扬草 (Fei Yangcao)	6–9	Relieve itching, lactogenesis	Cautiously used
69	Ferrous sulfate	Melanterite	绿矾 (Lv Fan)	0.8–1.6	Killing parasites	Cautiously used

	CHM (English)	CHM (Biological name)	CHM (Chinese)	Dose	Actions and clinical indications	Classification in pregnancy
70	Gendarussae herba	Gendarussa vulgaris Nees	小驳骨 (Xiao Bogu)	9–15	Furcture	Cautiously used
71	Haematitum	Haematitum	赭石 (Zhe Shi)	9–30	Liver yang over active, blurry vision and dizziness. Vomiting, hiccups, asthma; bleeding due to heat in the blood, excessive bleeding during menopause; chronic diarrhea; vagina yeast and bacterial infection; gastric neurosis	Cautiously used
72	I-borneolum/l-borneolum	Blumea balsamifera (L.) DC.	艾片 (Ai Pian)/ 左旋龙脑 (Zuo Xuanlongnao)	0.15–0.3	For fainting due to strokes or heat, bunacle, pain in joints, ulceration of the cornea, sores in the mouth, eczema, taking internally: mainly being used in pills; seldom in decoction. External application: for washing or added in external medication	Cautiously used
73	Impatientis semen	Impatiens balsamina L.	急性子 (Ji Xingzi)	3–5	Di gou cai (zhen zhu tou gu cao): rids of pain and dampness as in rheumatoid arthritis; invigorate blood, being used in rheumatoid arthritis, spastic muscles, eczema in the groin area, swollen boils, feng xian hua (feng xian tou gu cao): rids of pain and dampness as in rheumatoid arthritis, rid of toxin, being used in injuries, bruises, swelling, promoting menses, helping deliveries, expelling phlegm, tumors, snake and insect bites	Cautiously used
74	Leonuri herba	Leonurus japonicus Houtt.	益母草 (Yi Mucao)	9–40	As astringent, invigorate blood flow, promotes urination and rids of edema, rids of blood stasis, regulate menses, for premenstrual abdominal pain, infertility, post partum abdominal pain with lochioschesis (discharge in post delivery)	Cautiously used
75	Limonitum	Limonite	禹余粮 (Yu Yuliang)	9–15	Chronic diarrhea, bleeding not during menses, vagina discharge, hemorrhoids and hemorrhoids with bleeding or with pus	Cautiously used
76	Manis squama	Manis pentadactyla Linnaeus	穿山甲 (Chuan Shanjia)	5–10	Promote lactation, hastens boils to be ripen, expels pus, stop pain, pain in the joints of lower limbs, chronic malaria, rid of parasites. Unblocks menstruation, undo yu (blood stasis), acute mastitis, ridding of wind dampness bi	Cautiously used
77	Melanteritum	Ferrous sulfate heptahydrate	皂矾 (Zao Fan)	0.8–1.6	Rid of toxins and dampness: being used externally on boils, skin ulcers, skin fungal infection. As tonic and rid of parasites: being used in edema due to deficiency; parasites and pain in the abdomen	Cautiously used

	CHM (English)	CHM (Biological name)	CHM (Chinese)	Dose	Actions and clinical indications	Classification in pregnancy
78	Meliae cortex	Melia toosendan Sieb. et Zucc.; Melia azedarach L.	苦楝皮 (Ku Lianpi)	3–6	Promote qi flow, rid of dampness-heat, clear liver fire, rid of pain, promote urination, regulates qi, kills parasites. Also used externally for fungus infections of scalp. Ku lian pi should be cooked longer than other herbs in the formula, because the active ingredients are more difficult to dissolve in water	Cautiously used
79	Momordicae semen	Momordica cochinchinensis (Lour.) Spreng.	木鳖子 (Mu Biezi)	0.9–1.2	Similar as 36	Cautiously used
80	Moutan cortex	Paeonia suffruticosa Andr.	牡丹皮 (Mu Danpi)	6–12	Clears heat and cools the blood, clears fire of yin deficiency, clear blood stasis and rid of clots, drain pus and reduces swelling due to blood stasis	Cautiously used
81	Myrrha	Commiphora myrrha Engl.; Commiphora molmol Engl.	没药 (Mo Yao)	3–5	For pain due to injuries, bruises, rheumatoid arthritis, tumors in the uterus, hemorrhoid, cataract, amenorrhea, bone and muscle ache, angina pectoris. External use on inflammation of the mouth cavity, periodontitis, wounds from cut not healing, and pharyngitis	Cautiously used
82	Natrii sulfas	Mirabilitum	芒硝 (Mang Xiao)	6–12	1. Constipation with dark urine, fullness and pain in abdomen; 2. Conjunctivitis; 3. Boils in mouth and tongue; 4. Swollen and painful throat area; 5. Tumor of the breast; 6. Stopping lactation; 7. Worm parasites of small children; 8. Red, swollen boils, before breakage	Cautiously used
83	Natrii sulfas exsiccatus	Natrii Sulfas Exsiccatus	玄明粉 (Xuan Mingfen)	3–9	Similar as 82	Cautiously used
84	Notoginseng radix et rhizoma	Radix Notoginseng	三七 (San Qi)	1–9	Raw san qi can stop bleeding and can transform blood stasis. It can stop bleeding without causing blood clots. It is widely used in injury medicine as in broken bones, swelling, impact injuries. Cooked san qi can be used as tonic	Cautiously used
85	Olibanum	Boswellia carterii Birdw.; Boswellia bhaw-dajiana Birdw.	乳香 (Ru Xiang)	3–5	Improves circulation, repairs muscle, as resolvent. Being used in: pain due to blood clots, spastic muscle, carbuncles, gum bleeding, gingivitis, rheumatoid arthritis, cirrhosis of liver, amenorrhea, physical injuries, ulcerated wounds not healing	Cautiously used
86	Persicae semen	Prunus persica (L.) Batsch	桃仁 (Tao Ren)	5–10	Breaks up blood stasis for constipation due to dry intestines for early stage of liver cirrhosis inhibits epstein-barr virus anti-tumor	Cautiously used

	CHM (English)	CHM (Biological name)	CHM (Chinese)	Dose	Actions and clinical indications	Classification in pregnancy
87	Physochlainae radix	Physochlaina infundibu-laris Kuang	华山参 (Hua Shanshen)	0.1–0.2	Relieve cough, resolving phlegm	Cautiously used
88	Polygoni cuspidati rhizoma et radix	Polygonum cuspidatum Sieb. et Zucc.	虎杖 (Hu Zhang)	9–15	For jaundice, gall bladder stones, blood stasis with menses stoppage, yeast infection, rheumatoid arthritis, physical injuries from impacts, inflammation of the bronchi, lobar pneumonia, poisonous snake bites, scalding injuries, acute hepatitis, urinary tract infection, boils, stoppage of menses due to heat in the blood, breast cancer, menopausal bleeding disorder	Cautiously used
89	Pruni semen	Prunus japonica Thumb.	郁李仁 (Yu Liren)	6–10	Coprostasis	Cautiously used
90	Psammosilenes radix	Psammosilene tunicoides W.C. Wu et C.Y. Wu	金铁锁 (Jin Tiesuo)	0.1–0.3	Pain control	Cautiously used
91	Rhapontici radix	Rhaponticum uniflorum (L.) DC.	漏芦 (Lou Lu)	5–9	Similar as 67	Cautiously used
92	Rhei radix et rhizoma	Rheum palmatum L.	大黄 (Da Huang)	3–15	Lack of bowel movement, dysentery, blood clots, tumor, red and painful eyes, abdominal distention and/or pain, blood in stool, hemorrhoidal bleeding, urination burning sensation, nose bleeding, coughing up blood, sore extremities, edema, jaundice, lesions, burns and scalding (external application), absence of menses. Note: cooking for more than 10 minutes will reduce its purgative effect. For purgative effect use raw da huang. For blood invigorating action use wine or vinegar treated da huang. To stop bleeding use charred da huang	Cautiously used
93	Sappan lignum	Caesalpinia sappan L.	苏木 (Su Mu)	3–9	For vomiting, hiccups, burping, indigestion, and flatulence due to pixu (spleen deficient) or fungal infection; and for difficulty in expelling phlegm; chronic bronchitis; injuries from impact, dysentery, tetanus	Cautiously used

	CHM (English)	CHM (Biological name)	CHM (Chinese)	Dose	Actions and clinical indications	Classification in pregnancy
94	Selaginellae herba	Selaginella tamariscina (Beauv.) Spring	卷柏 (Juan Bai)	5-10	Improves circulation	Cautiously used
95	Sennae folium	Cassia angustifolia Vahl	蕃泻叶 (Fan Xieye)	2-6	Coprostasis	Cautiously used
96	Sulfur	Surphur	硫黄 (Liu Huang)	1.5-3	Coprostasis, killing parasite	Cautiously used
97	Tetrapanax medulla	Tetrapanax papyrifer (Hook.) K. Koch	通草 (Tong Cao)	3-5	Being used in typhoid, paratyphoid with dark urine, pain in gonorrhea, edema scanty urine, and lack of mother's milk	Cautiously used
98	Trichosanthis radix	trichosanthes kirilowii Maxim.; trichosanthes rosthornii Harms	天花粉 (Tian Huaafen)	10-15	Clears lung heat, dissolves phlegm, for cough with thick phlegm, rid of toxicity, expels pus; for treatment of chlorion epithelioma, hydatidiform mole	Cautiously used
99	Typhae pollen	Typha angustifolia L.	蒲黄 (Pu Huang)	5-10	Hei pu huang is pu huang that has been stir fried till dark color. It is being used in stopping bleeding. Raw pu huang possesses double effects of stopping bleeding and promoting circulation. For treatment of: angina: blood clot in the brain, high blood lipids, inflammation of the intestine and difficulty in urination: pu huang 50 g, xiong huang 10 g, bing pian 3 g, fresh white part of green onion 200 g, (wash the part of green onion and boil in water for 3 minutes. Smash all herb past it to the lower abdomen while still warm. Bleeding and abdomen ache due to chronic colitis: pu huang 3 g, wu ling zhi 3 g (wrap in cloth), baked ge gen 10 g, baked rou dou kou 3 g. Make into decoction and use as tea. External injury of the head with swelling: use raw pu huang and apply to the injury, 3 times a day. Bleeding in external injuries, hemorrhoids, boils, inflammation of the rib cartilage (without pus), rash in babies	Cautiously used
100	Typhonii rhizoma	Typhonium giganteum Engl.	白附子 (Bai Fuzi)	3-6	Similar as 2	Cautiously used
101	Vaccariae semen	vaccariae segetalis (Neck.) Garcke	王不留行 (Wang Buliuxing)	5-10	Promote diuresis	Cautiously used

	CHM (English)	CHM (Biological name)	CHM (Chinese)	Dose	Actions and clinical indications	Classification in pregnancy
102	Wenyujin rhizoma concisum	Curcuma wenyujin Y.H. Chen et C. Ling	片姜黄 (Pian Jianghuang)	3–9	Actions and indications: improves circulation of blood and qi, promotes flow of menses and relieves pain. For wind chill induced shoulder pain, mood fluctuations, schizophrenia, fever with dizziness, vomiting blood, nose bleeding, blood in urine, bleeding not during menses, jaundice, lower back pain, chest and abdomen pain caused by blood stasis, flatulence, pain during period of menses, injuries, bruises and swelling. Angina, treatment of pain in the rib area, gallbladder stones, postpartum pain. Today's application: high lipids, angina pectoris, rheumatoid arthritis, inflammation after surgery, periodontitis, tumor, acid dyspepsia, flatulent dyspepsia, atonic dyspepsia, shingles/herpes zoster, herpes simplex, coronary atherosclerosis, for inhibiting building up of b-amyloid, leukemia	Cautiously used

Similar: the clinical application and or the therapeutical effects of these CHMs are similar.

Same: (1) The CHMs are origin from different parts of a same plant or animal. (2) The CHMs are origin from the same part of the same plant or animal, but prepared in a different way for clinical medications.

Table 1. Summary of 105 CHMs for pregnancy [15, 16].

3.3.6. Data extraction, evaluation and management

Extraction form was designed and used to extract data. For eligible studies, two review authors extracted the data, any discrepancy was resolved through discussion or the third person was consulted. For each selected literature, publication year, study population, participant numbers, maternal age, gestation age, symptoms and signs, clinical diagnosis, examination and laboratory results, disease course, study intervention, standard or modified Chinese medicine formulas, individual medicine, immediate and follow-up outcomes were recorded. But only the data related to the safety classification and adverse outcomes would be reported in this review.

4. Results

4.1. Chinese pharmacopeia and literature study

There were 105 CHMs in Chinese pharmacopeia remarked with potential toxicity classification for pregnant women, of which 38 were “contraindicated”, 2 were “not recommended” and 65 were “cautiously used” during pregnancy. Three of them were repeated under different common names, so we studied and collected information of 102 CHMs (**Table 1**) [15]. Some of the CHMs were origin from the same part of a plant, but they were prepared and applied in different format. Although their properties and safety outcomes were similar, we kept them separately list in the summary table.

An extension search on the cited references was carried out, and data of around another 600 studies were further extracted [15, 16]. A summary included the common name (English name), the biological name (Latin name), the original name (Chinese name), the recommended dose range in Chinese Pharmacopeia, clinical effects/indications and the safety classification in pregnancy of these 102 CHMs was reported in **Table 1**.

4.2. Adverse outcomes

4.2.1. General adverse effects and lethal effects

Among these 102 CHMs for pregnancy, around 80% were reported with their safety in clinical trials and or animal studies.

In those 38 “contraindicated” CHMs, 28 (73.7%) of which reported either general adverse effects or lethal effects (**Table 2**). About 16 of 38 (42.1%) CHMs were recorded with general adverse outcomes such as gastrointestinal discomfort including nausea, vomiting, lethargy, abdominal pain, diarrhea; nervous system problems such as drowsiness, headache, dizziness, respiratory failure, shock, dermatitis and ulcers, damage to multi-organ/systems, and so on. About 18 of 38 (47.4%) CHMs were recorded with lethal effects in human and mammals like mice, rats and rabbits. Immediate death was reported when Realgar Tragacanth (a component of Realgar) was orally administrated to mice, but details of the dose and dosing were not reported.

No.	CHM (English)	Adverse outcomes		Reproductive adverse outcomes	
		General adverse effects	Lethal effects	Maternal effects	Fetal effects
1	Aconiti kusnezoffii radix				
2	Aconiti radix		Death (human, po, 2–5 mg component)		
3	Anemones raddeanae rhizoma				
4	Aristolochiae fructus		Death (rabbit, ip, other details not available)	Stimulation on uterine muscle	
5	Aristolochiae herba				
6	Calomelas	Necrosis in multiple organs: heart, kidney, liver, lung, ovary (animals)			
7	Cinnabaris	Damage to heart, liver and kidney (mice, po, component 9.5 g/kg)		Decrease of pregnancy rate (mice, po)	
8	Crotonis fructus	1. Inducing dermatitis; 2. Sore throat, abdominal pain, watery diarrhea or bloody mucus, cyanosis, shock (human and animals)	Death (human, po, 20 drops)		
9	Crotonis semen pulveratum				
10	Curcumae rhizoma			Anti-pregnancy effect: interfere with implantation	Affect fetal growth
11	Daturae flos	Chromosome damage			
12	Erycibe schmidtii	1. Chronic toxicity on nervous system (mice); 2. Cardiac arrhythmias and death (rabbit, details not available)		Inhibition effects on uterus (pregnant rats)	
13	Euphorbiae pekinensis radix	Dermatitis	Death	Stimulation on pregnancy uterus	
14	Euphorbiae semen	1. Diarrhea; 2. Persistent abdominal pain, nausea, vomiting, lethargy, drowsiness (human)	Death (human)		

No.	CHM (English)	Adverse outcomes		Reproductive adverse outcomes	
		General adverse effects	Lethal effects	Maternal effects	Fetal effects
15	Euphorbiae semen pulveratum	1. Diarrhea; 2. Persistent abdominal pain, nausea, vomiting, lethargy, drowsiness (human)	Death (human)		
16	Eupolyphaga steleophaga				
17	Ferulae resina			1. Termination of pregnancy: induce miscarriage (pregnant mice, po, component 180 mg/kg); 2. Stimulation on pregnancy uterus (rabbit and mice)	
18	Genkwa flos			Termination of pregnancy: 1. Induce miscarriage (pregnant monkeys, amniotic injection for 1–3 days, component 0.2–8 mg); 2. Stimulation on pregnancy uterus (rabbit)	
19	Gleditsiae fructus abnormalis	1. Hemolysis; 2. Local mucosal irritation, damage to central nervous system, respiratory failure, death (mammals)	Death (mammals)		
20	Ground beetle				
21	Hirudo			1. Termination on pregnancy: 1.25 g/kg; 2. Termination on pregnancy: (ih on pregnancy d1, d6, d10, bid, decoction 2.5–3 g/kg)	
22	Hydrargyri oxydum rubrum		Death (component HgO ₃)		
23	Hyoscyami semen	Chromosome damage			
24	Kansui radix	Hemolysis effect on quadriceps (rabbit)	Anti-fertility effects: placenta damage, miscarriage	1. Recorded embryotoxicity, but no malformation on fetus (rabbit, details not available); 2. Interfere with fetal circulation system	

No.	CHM (English)	Adverse outcomes		Reproductive adverse outcomes	
		General adverse effects	Lethal effects	Maternal effects	Fetal effects
25	Moschus		Death (mice, iv)	1. Stimulation on uterus, esp. Later stage of pregnancy (rabbit, puinea pig, rat); 2. Anti-early pregnancy and anti implantation	
26	Mylabris	1. Poisoning dogs and mice were liver and kidney damage (dogs and mice); 2. Acute poisoning of digestive, kidney, nervous system symptoms, such as blisters, ulcers, nausea and vomiting, oliguria, hematuria, dysuria, dizziness, blurred vision, high fever, shock and other symptoms (human, po)		Death (human, po, 3 g)	
27	Nigellae semen				
28	Papaveris pericarpium	1. Headache, dizziness, nausea and vomiting, constipation, urinary urgency and dysuria, sweating, biliary colic, the risk for respiratory depression; 2. Acute poisoning as lethargy, miosis, respiratory depression; 3. Infant poisoning can occur convulsions (human)			
29	Pharbitidis semen	Under large dose (animals): 1. Gastrointestinal irritation symptoms such as vomiting, abdominal pain, diarrhea, bloody mucus; 2. Kidney stimulation symptoms such as severe hematuria; 3. Nervous system such as language barrier, coma		Stimulation on pregnancy uterus (rat)	

No.	CHM (English)	Adverse outcomes		Reproductive adverse outcomes	
		General adverse effects	Lethal effects	Maternal effects	Fetal effects
30	Phytolaccae radix	Vomiting (cat, po, 2.5–10 g/kg), damage to brain (mice, po)			
31	Realgar		Immediate death (mice, po, component)		
32	Rhododendri mollis flos	Dermatitis	Death		
33	Scolopendra		Death (mice, intraperitoneal injection of high dose)		
34	Scorpio		Death (rabbit, iv, 0.5 mg/kg)	Specific toxicity: fetal malformation on bone development	
35	Sparganii rhizoma		Death (mice, ip for 7 days)	Stimulation on uterus (pregnant rabbits)	
36	Strychni semen		1. Death (mice, details not available); 2. Death (human, po, 30 mg)		
37	Strychni semen pulveratum		1. Death (mice, details not available); 2. Death (human, po, 30 mg)		
38	Toxicodendri resina				
39	Gleditsiae sinensis fructus	Chronic toxicity (mammal, po)	Death (human, po)		
40	Saussureae involucratae herba				
41	Abelmoschi corolla				
42	Achyranthis bidentatae radix			1. Stimulation on non-pregnancy and early pregnancy uterus (mice); 2. Inhibition effects on both non-pregnancy and early pregnancy uterus (guinea pig); 3. Anti-fertility effect on pregnancy (mice)	
43	Aconiti kusnezoffii folium				
44	Aconiti kusnezoffii radix cocta				

No.	CHM (English)	Adverse outcomes		Reproductive adverse outcomes	
		General adverse effects	Lethal effects	Maternal effects	Fetal effects
45	Aconiti lateralis radix praeparata				
46	Aconiti radix cocta				
47	Aloe	1. local muscle necrosis (dog, muscle injection, high dose of decoction); 2. abdominal pain and pelvic congestion, nephritis.			
48	Arisaematis rhizoma	1. Weight loss, weakness, death, the water decoction of rabbit conjunctival irritation; 2. Emetic effect (mice, po, raw herb 40 g/kg)	Death (rabbit)		
49	Arisaematis rhizoma preparatum				
50	Aurantii fructus			1. Stimulation effects on uterus (rabbit); 2. Inhibition effects on uterus (mice)	
51	Aurantii fructus immaturus	Gastrointestinal expansion and salivate phenomenon (some animals, po)		1. Stimulation effects on uterus (rat and rabbit); 2. Inhibition effects on uterus (mice)	
52	Borneolum	1. Chronic toxicity to peripheral blood parameters and organ weight effects; 2. Liver damage (rat, po, 5 g/kg); 3. Neurotoxic effects (rat, po, 5 g/kg)		1. Induced abortion (mice, intraperitoneal injection once, 1/4,1/8,1/16ld50, either in early pregnancy (7–9d), mid pregnancy (10–14d) and late pregnancy (16–18d)) 2. Induction effect in mid and late pregnancy (mice)	
53	Borneolum syntheticum	1. Chronic toxicity to peripheral blood parameters and organ weight effects; 2. Liver damage (rat, po, 5 g/kg); 3. Neurotoxic effects (rat, po, 5 g/kg)		1. Induced abortion (mice, intraperitoneal injection once, 1/4,1/8,1/16ld50, either in early pregnancy (7–9d), mid pregnancy (10–14d) and late pregnancy (16–18d)) 2. Induction effect in mid and late pregnancy (mice)	

No.	CHM (English)	Adverse outcomes		Reproductive adverse outcomes	
		General adverse effects	Lethal effects	Maternal effects	Fetal effects
54	Bovis calculus	Fewer activities (mice, po, 7.5 g/kg)		Stimulation effects on pregnancy uterus and anesthesia uterus (rabbit, 0.9 mg component)	
55	Bovis calculus artifactus				
56	Bovis calculus sativus				
57	Bufonis venenum				
58	Campsis flos			1. Inhibition effects on mice non-pregnancy uterus (mice, 7.5 mg/ml); 2. Stimulation effects on pregnancy uterus	
59	Carthami flos	Low-spirited poisoning symptoms, reduced activity, walking difficulties (mice, intragastric and intraperitoneal injection, decoction)	Death (mice, intraperitoneal injection, component)	Stimulation effects on uterus (more obvious on pregnancy uterus than non-pregnancy one)	
60	Cinnamomi cortex				
61	Cinnamomi ramulus	The toxic effects of guizhi on mice have significant differences between day and night, the daytime toxic and lethal effects were significantly enhanced at night (mice)			
62	Coicis semen				
63	Croci stigma	Death (mammals)	Death (mammals)	Stimulation effects on both non pregnancy and pregnancy uterus (mice, puinea pig, rabbit, god, cat)	
64	Cyathulae radix			1. Stimulation effects on pregnant uterus (rabbit and cat); 2. Miscarriage rate 100% (mice, po for 7 days, component 2.5 g/kg)	
65	Dianthi herba			Stimulation on pregnancy uterine (rabbit and rat)	

No.	CHM (English)	Adverse outcomes		Reproductive adverse outcomes	
		General adverse effects	Lethal effects	Maternal effects	Fetal effects
66	Dichroae radix				
67	Echinopsis radix				
68	Euphorbiae hirtae herba			Increase miscarriage rate (pregnant mice, iv, 1.2 mg/kg on d8, d12 or d16)	
69	Ferrous sulfate	Vomiting, abdominal pain, diarrhea, dizziness and other adverse reactions			
70	Gendarussae herba				
71	Haematitum	Liver and lung damage (mice, po, 15–30% decoction)			
72	I-borneolum	1. Chronic toxicity to peripheral blood parameters and organ weight effects; 2. Liver damage (rat, po, 5 g/kg); 3. Neurotoxic effects (rat, po, 5 g/kg)		1. Induced abortion (mice, intraperitoneal injection once, 1/4,1/8,1/16ld50, either in early pregnancy (7–9d), mid pregnancy (10–14d) and late pregnancy (16–18d)); 2. Induction effect in mid and late pregnancy (mice)	
73	Impatientis semen			1. Anti-fertility effects (mice, po, decoction 3 g/kg); 2. Stimulation effects on uterus (mice, puinea pig and rabbit)	
74	Leonuri herba			1. Stimulation effects on uterus (mice, guinea pig, rabbit, dog, po, decoction and components); 2. Anti implantation and anti early pregnancy (mice, po, 0.1 ml for 4–5 times)	
75	Limonitum	Antifeedant, pulmonary congestion, hepatomegaly (mice, iv, decoction)			
76	Manis squama				
77	Melanteritum				
78	Meliae cortex	Stomach damage (rats) and inflammation (dogs)	Death (dogs, rabbits, monkeys, po, component)		
79	Momordicae semen				

No.	CHM (English)	Adverse outcomes		Reproductive adverse outcomes	
		General adverse effects	Lethal effects	Maternal effects	Fetal effects
80	Moutan cortex	Some central inhibition such as temperature decreasing, reflection disappeared, reduced activity, reduced respiratory, etc. (mice, intraperitoneal injection, component)			
81	Myrrha				
82	Natrii sulfas	Death (mice, intraperitoneal injection, decoction)	Death (mice, intraperitoneal injection, decoction)		
83	Natrii sulfas exsiccatus	Induce cancer			
84	Notoginseng radix et rhizoma	Acute and chronic toxicity reported, but details not available			
85	Olibanum				
86	Persicae semen	Visible muscle relaxation, ataxia, piloerection and other phenomena (mice, intraperitoneal injection of 3.5 g/kg decoction)		Stimulation on pregnant uterine	
87	Physochlainae radix	Reduced activity, but recover on the next day (mice, intraperitoneal injection, 1 g/ml water extract)			
88	Polygoni cuspidati rhizoma et radix	Different degree of peritonitis, the severity and scope and dosage showed parallel effects, 700 mg/kg dose group was administered after 6 weeks can cause white blood cell count was significantly reduced, but there were no significant changes in blood and liver and kidney function. (rats, intraperitoneal injection, component)			

No.	CHM (English)	Adverse outcomes		Reproductive adverse outcomes	
		General adverse effects	Lethal effects	Maternal effects	Fetal effects
89	Pruni semen				
90	Psammosilenes radix				
91	Rhapontici radix				
92	Rhei radix et rhizoma	1. Long-term toxicity like cirrhosis and electrolyte metabolism (mice, po); 2. Overdose causes poisoning, nausea, vomiting, dizziness (mice, po).			
93	Sappan lignum				
94	Selaginellae herba				
95	Sennae folium				
96	Sulfur	1. Antifeedant and hepatomegaly (mice, po, decoction); 2. Overdose causes sulfur, central nervous damage and death (mice, po)	Death (mice, po, overdose)		
97	Tetrapanacis medulla				
98	Trichosanthis radix	1. Allergies (human, animals); 2. General toxicity: loss of appetite, damage to heart, liver and kidney, and central nervous system, death (female dog, im, 0.2–2 mg/kg)	Death (female dog, im, 0.2–2 mg/kg)	1. Miscarriage; 2. Stimulation effects on pregnant uterus (rabbit)	
99	Typhae pollen	1. Allergic reaction (guinea pig, intraperitoneal injection, decoction); 2. Hemolysis; 3. Reduction of red blood cells and white blood cells (mice)		1. Stimulation effects on uterus (mice, rat, puinea pig, rabbit) 2. Induction effects (puinea pig, mice, intraperitoneal injection, 50% dedcoction 3–2 g/kg) 3. Induced abortion (mice, po, decoction 10–20 g/kg)	Induced fetal death (mice, po, decoction 10–21 g/kg)
100	Typhonii rhizoma	Difficulty breathing, reduced activity, individual animal death (mice, po, decoction)	Individual animal death (mice, po, decoction)		

No.	CHM (English)	Adverse outcomes		Reproductive adverse outcomes	
		General adverse effects	Lethal effects	Maternal effects	Fetal effects
101	Vaccariae semen			1. Anti-implantation and decrease pregnancy rate; 2. Stimulation on pregnant uterus (rat)	
102	Wenyujin rhizoma concisum			1. Anti-fertility effects; 2. Anti-pregnancy effects: termination of pregnancy; 3. Stimulation on uterus (mice, puinea pig, rabbit)	

Table 2. Adverse outcomes of CHMs for pregnancy [15, 16].

In 2 “not recommended for pregnancy” CHMs (**Table 2**), *Gleditsiae Sinensis Fructus* (*Moschus berezovskii* Flerov, *DaJiaoZao*) was recorded with both general effects of chronic toxicity in oral administration to mammals and lethal effects when human took a higher dose. No obvious adverse effects were recorded to the other CHM, *Saussureae Involucratae Herba* (*Saussurea involucrata* (Kar.et Kir.) Sch.-Bip., *TianShanXueLian*). Although it has great therapeutical function of improve the immune system, due to its pharmacological effects to enhance the blood circulation and stimulate the contraction of uterus, it may induce abortion during pregnancy, so it was not recommended for pregnant women.

In 65 “cautiously used” CHMs, 33 (50.8%) of which reported either general adverse effects or lethal effects (**Table 2**). About 24 of 65 (36.9%) CHMs were recorded with same general adverse outcomes such as gastrointestinal discomfort, nervous system problems, skin disorders and multi-organ damage. Other adverse effects such as muscle necrosis, pelvic congestion and cancer were also recorded. A total of 9 of 38 (13.8%) CHMs were recorded with lethal effects in human and mice. One study also reported that *Meliae Cortex* (*Melia toosendan* Sieb.et Zucc.; *Melia azedarach* L, *KuJianPi*) could cause death of rabbits, dogs and monkeys after oral administration of high dose of *Toosendanin* (a component), and the main reason is visceral bleeding, decreased blood pressure then acute circulatory failure.

4.2.2. Maternal and fetal adverse effects

Generally speaking, more maternal adverse effects were recorded than fetal effects. But this may be due to the failure of early pregnancy of mothers.

In those 38 “contraindicated” CHMs, 2 (5.3%) of which reported adverse effects on both mothers and fetuses (**Table 2**). A total of 12 of 38 (31.6%) CHMs were recorded with maternal adverse outcomes such as lower pregnancy rate (mainly due to anti-implantation), miscarriage (mainly due to effects on uterus), placenta damage and so on. About 3 of 38 (7.9%) CHMs were recorded with fetal adverse effects on bone development, circulation system and malformation.

No obvious maternal and fetal adverse effects were reported in those two “not recommended for pregnancy” CHMs (**Table 2**).

In those 65 “cautiously used” CHMs, 1 (1.5%) of which reported adverse effects on both mothers and fetuses (Table 2). About 20 of 65 (30.8%) CHMs were recorded with same maternal adverse outcomes as the “contraindicated” CHMs, and the study animals included mice, guinea pigs, rats and rabbits. Only 1 of 65 (1.5%) CHMs, Typhae Pollen (*Typha angustifolia* L, PuHuang), was recorded with mouse fetal death under oral administration of a 10–21 g/kg decoction.

4.3. Animal toxicity data

In Table 3, we summarized the toxicity data of those 102 CHMs from different animal studies and provided the information of LD50, dose, doing and species [15]. About 21 of 102 (20.6%) CHMs have more than one LD50 data, by applying raw herb, main/active components, water extraction and decoction or applying different species of animals. But 35 of 102 (34.3%) CHMs did not have a LD50 record. One implied reason is the CHM is too safe to test a LD50 data. Another reason is that half of these CHMs without a LD50 data were mineral origin, and there have been no study carried out to test their LD50 so far.

No.	CHM (English)	LD50	Dosing	Species	Remarks
1	<i>Aconiti kusnezoffii</i> radix	1.62–5780 mg/kg ⁴	po, ip	Mouse	
2	<i>Aconiti radix</i>	0.3–18.0 mg/kg ^{1,4}	ig, iH	Mouse	
3	<i>Anemones raddeanae</i> rhizoma				
4	<i>Aristolochiae fructus</i>				
5	<i>Aristolochiae herba</i>	0.02 g/kg ¹	iv	Mouse	
6	<i>Calomelas</i>	410–2068 mg/kg ²	ig	Mouse	
6	<i>Calomelas</i>	1740 mg/kg ²	ig	Rat	
7	<i>Cinnabaris</i>	12.10 g/kg ²	iv	Mouse	
8	<i>Crotonis fructus</i>	50–80 mg/kg ¹	iH	Rabbit	
8	<i>Crotonis fructus</i>	1 g/kg ¹	po	Rat	
8	<i>Crotonis fructus</i>	1600 mg/kg ⁴	po	Mouse	
8	<i>Crotonis fructus</i>	600 mg/kg ¹	iH	Guinea pig	
9	<i>Crotonis semen pulveratum</i>				
10	<i>Curcumae rhizoma</i>	86.8 g/kg ^{1,4} raw herb	po	Mouse	
11	<i>Daturae flos</i>	8.2 mg/kg injection	iv	Mouse	
12	<i>Erycibe schmidtii</i>	6.22–8.85 mg/kg ¹	iH	Mouse	
13	<i>Euphorbiae pekinensis</i> radix				

No.	CHM (English)	LD50	Dosing	Species	Remarks
14	Euphorbiae semen				
15	Euphorbiae semen pulveratum				
16	Eupolyphaga steleophaga	146.45 mg/kg ¹	ip	Mouse	
17	Ferulae resina				
18	Genkwa flos	9.25 g/kg ²	ip	Rat	
18	Genkwa flos	1.0–17.78 g/kg ^{1,2}	ip, ig	Mouse	
19	Gleditsiae fructus abnormalis				
20	Ground beetle	146.45 mg/kg ¹	ip	Mouse	
21	Hirudo	15.28 g/kg ²	iH	Male mouse	Mouse, po, qd, decoction 500 and 1000 mg/kg, lower maternal weight, higher resorption rate, fetal malformation rate, higher neonatal mortality
22	Hydrargyri oxydum rubrum	22–120.98 mg/kg ^{1,2}	ig	Mouse	
22	Hydrargyri oxydum rubrum	18 mg/kg ¹	ig	Rat	0.1–1.5 g HgO ₂ to human, death
23	Hyoscyami semen				
24	Kansui radix	30–346.1 mg/kg ¹	ip	Mouse	
25	Moschus	152–848 mg/kg ¹	ip, iv	Mouse	
26	Mylabris	1.71–1037 mg/kg ^{1,2}	ig, ip, iv	Mouse	
27	Nigellae semen				
28	Papaveris pericarpium	64–600 mg/kg ¹	iH, ip, po	Rat	
28	Papaveris pericarpium	20–745 mg/kg ¹	iH, ip, po, iv	Mouse	
28	Papaveris pericarpium	18–2200 mg/kg ¹	iH, iv, po	Rabbit	
28	Papaveris pericarpium	160–237 mg/kg ¹	po, ip	Guinea pig	
28	Papaveris pericarpium	MLD 60 mg/kg	iH	Cat	
29	Pharbitidis semen	37.5 mg/kg ¹	lh	Mouse	
30	Phytolaccae radix	11.87–486 mg/kg ^{1,2}	ig, ip, iv	Mouse	
31	Realgar	3.207 g/kg	ig	Mouse	
32	Rhododendri mollis flos	0.25–5850 mg/kg ^{1,2}	ig, po, iv, ip, iH	Mouse	
33	Scolopendra	22.5–9900 mg/kg ^{1,2}	ig, ip	Mouse	

No.	CHM (English)	LD50	Dosing	Species	Remarks
34	Scorpio	2.4–10.3 g/kg ^{1,2}	iv, ip	Mouse	
35	Sparganii rhizoma	55.8–233.3 g/kg ³ raw herb	ip	Mouse	
36	Strychni semen	1.53–301.9 mg/ kg ^{1,2,4}	ig, ip	Mouse	
37	Strychni semen pulveratum	301.9 mg/kg ²	ig	Mouse	
38	Toxicodendri resina				
39	Gleditsiae sinensis fructus				
40	Saussureae involucratae herba				
41	Abelmoschi corolla				
42	Achyranthis bidentatae radix	6.4–146.49 g/kg ¹	ig, ip	Mouse	
43	Aconiti kusnezoffii folium				
44	Aconiti kusnezoffii radix cocta				
45	Aconiti lateralis radix praeparata	0.1–17400 mg/kg ^{1,2}	ig, iv, ip, Ih	Mouse	
45	Aconiti lateralis radix praeparata	0.102 mg/kg (minimum lethal dose)	iv	Rat	
45	Aconiti lateralis radix praeparata	0.075–1.65 mg/kg ¹	iv	Frog	
45	Aconiti lateralis radix praeparata	0.04–0.05 mg/kg ¹	iv	Rabbit	
45	Aconiti lateralis radix praeparata	0.06–0.12 mg/kg ¹	iv	Guinea pig	
46	Aconiti radix cocta				
47	Aloe				
48	Arisaematis rhizoma	13.5–210 g/kg ^{1,2,4}	ig, ip	Mouse	
49	Arisaematis rhizoma preparatum				
50	Aurantii fructus				
51	Aurantii fructus immaturus	71.8–267 g/kg ²	iv, ip	Mouse	
52	Borneolum	907–4960 mg/kg ¹	ig, ip	Mouse	

No.	CHM (English)	LD50	Dosing	Species	Remarks
53	Borneolum syntheticum	907–4960 mg/kg ¹	ig, ip	Mouse	
54	Bovis calculus	497.5–6630 mg/kg ¹	ig, ip, iv	Mouse	
55	Bovis calculus artifactus				
56	Bovis calculus sativus				
57	Bufois venenum				
58	Campsis flos	50 g/kg (raw herb, maximum tolerated dose)	ig	Mouse	
59	Carthami flos	2.35–20.7 g/kg ^{1,2}	ig, ig, iv	Mouse	
60	Cinnamomi cortex	42–46 g/kg ^{1,2}	ip	Mouse	
61	Cinnamomi ramulus	624.7(daytime)–773.6(night)mg/kg ²	ig	Mouse	
62	Coicis semen	10 ml/kg ¹ (maximum tolerated dose)	po	Mouse	
63	Croci stigma	20.7 g/kg ¹	po	Mouse	
64	Cyathulae radix				
65	Dianthi herba				
66	Dichroae radix				
67	Echinopsis radix				
68	Euphorbiae hirtae herba				
69	Ferrous sulfate				
70	Gendarussae herba				
71	Haematitum	12.90 g/kg ²	iv	Mouse	
72	I-borneolum	907–4960 mg/kg ¹	ig, ip	Mouse	
73	Impatiens semen				
74	Leonuri herba	0.572–60 g/kg ^{1,2}	iv	Mouse	
75	Limositum	8.25 g/kg ²	iv	Mouse	
76	Manis squama				
77	Melanteritum				
78	Meliae cortex	13.8–244.2 mg/kg ¹	ip, iv, iH, po	Mouse	
78	Meliae cortex	9.8 mg/kg ¹	iH	Rat	
78	Meliae cortex	4.2 mg/kg ¹	iv	Rabbit	
79	Momordicae semen				

No.	CHM (English)	LD50	Dosing	Species	Remarks
80	Moutan cortex	196–6900 mg/kg ¹	ig, iv, ip	Mouse	
81	Myrrha				
82	Natrii sulfas	6.738 g/kg ²	ip	Mouse	
83	Natrii sulfas exsiccatus				
84	Notoginseng radix et rhizoma	33≥5000 mg/kg ^{1,2}	ih, ivgtt, ip, po	Mouse	
84	Notoginseng radix et rhizoma	498 mg/kg ¹	ivgtt	Guinea-pig	
85	Olibanum				
86	Persicae semen	222.5 g/kg ²	ip	Mouse	
87	Physochlainae radix	43 g/kg ²	ip	Mouse	
88	Polygoni cuspidati rhizoma et radix	249.5–1000 mg/kg ¹	ip	Mouse	
89	Pruni semen				
90	Psammosilenes radix				
91	Rhapontici radix				
92	Rhei radix et rhizoma	0.56–153.5 g/kg ^{1,2}	po	Mouse	
93	Sappan lignum	18.9 g/kg ²	ip	Mouse	
94	Selaginellae herba				
95	Sennae folium	1.414 g/kg ¹	ip	Mouse	
96	Sulfur	0.266 g/kg ¹	ig	Mouse	
97	Tetrapanacis medulla				
98	Trichosanthis radix	0.236–2.26 mg/each animal ¹	iH	Mouse	
99	Typhae pollen	35.57 g/kg ²	ip	Mouse	
100	Typhonii rhizoma	29.57–32.58 g/kg ^{1,4}	iv	Mouse	
101	Vaccariae semen				
102	Wenyujin rhizoma concisum				

¹Main component (s).

²Herbal water extraction.

³Decoction.

⁴Raw herb.

ip: peritoneal injection; ig: intragastrical administration; iv: intravenous injection; iH: hypodermic injection; po: oral administration; im: intramuscular injection.

Table 3. Animal toxicity data of CHMs for pregnancy [15, 16].

5. Conclusions and recommendations

5.1. Chinese medicines are not free of risk

The active ingredients of the Chinese medicines are chemicals that are similar to prescribed drugs. Chinese medicines are not free of risk and they have the same potential to cause adverse effects.

In this overview of Chinese medicines for pregnancy with well-characterized reproductive toxicity, though these Chinese medicines are not commonly used in clinical practice, some of them could result in severe consequences when given in over dosages or even normal dosages. In the communities which use Chinese medicines, special attention should be paid and precautions should be taken to prevent mistaken overdoses of the Chinese medicines.

5.2. International guideline is necessary

It should be acknowledged that some of the studies from animals may not be comparable to human responses, both referring to Chinese medicines and Western medicines. Despite variations in clinical practice and therapeutic prescription, Chinese medication in Traditional Chinese Medicine should comply with modern pharmacological principles as in Western Medicine. Chinese medicines may be beneficial but may also adversely affect both mothers and fetuses in utero. International regulations have not been designed or specified to categorize the Chinese medicines for use in pregnancy. Until now, no detailed/well-designed reproductive toxicity and pharmacotoxicity studies are available to assess the potential risk of Chinese medicines during pregnancy, as much as true that conventional medications are not well tested in pregnancy too.

Before the detailed studies become available, here we take the initiative in gathering information about the adverse effects and potential toxicity of the Chinese medicines for pregnancy from Chinese Pharmacopeia and the extensive literature studies.

5.3. Recommendations

We hope more comprehensive and systematic experiments will be carried out. Until more reliable and scientific research data become available, clinicians should appraise both the risk and benefit before recommendations to pregnant women or women who plan to be pregnant. Both Chinese and Western physicians should explicitly elicit and document the history of the use of any Chinese medications. This is to prevent and recognize potential serious problems associated with their use and should encourage their discontinuation. More studies and clinical trials in humans with a larger sample size are obviously mandatory. We do recommend more systematic basic investigation of the safety use of Chinese medicines for pregnancy.

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