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REVIEW ARTICLE

Traditional preparations used as uterotonics in Sub-Saharan Africa and their pharmacologic effects

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ABSTRACT

Background: Little is known about the use of traditional preparations for uterotonic effects at or near delivery in Sub-Saharan Africa. *Objective:* To describe (1) use of traditional preparations in Sub-Saharan Africa intended to have uterotonic effects at or near birth; and (2) results of pharmacologic investigations of the uterotonic properties of such preparations. *Search strategy:* Structured review of 13 databases. *Selection criteria:* Articles describing use of traditional preparations in Sub-Saharan Africa with primary data, published in English between January 1, 1980 and June 30, 2010. *Data collection and analysis:* Full-text review using standard spreadsheet templates. *Main results:* Objective 1 analysis identified 208 plant species used for uterotonic effects at or near delivery. The most common use was labor induction/augmentation (n = 185). Other uses were to expel the placenta, shorten the third stage of labor, manage retained placenta (n = 61), and prevent/manage postpartum hemorrhage (n = 20). Objective 2 analysis identified 82 species with uterotonic activity confirmed through pharmacologic evaluation. Studies also identified potentiating/inhibiting effects of extracts on pharmaceutical uterotonics. *Conclusion:* Numerous plants are used for uterotonic effects in Sub-Saharan Africa; uterotonic activity has been confirmed in many through pharmacologic evaluation. Such use may increase the risk of adverse outcomes. Further research is needed on the uterotonic efficacy of traditional preparations and on interventions to address use during labor.

1. Introduction

Around 350 000 women die of maternal causes annually [1,2]. Most of these deaths occur in low-resource countries, and nearly three-fifths in Sub-Saharan Africa [2]. The most common cause of maternal mortality in Sub-Saharan Africa is obstetric hemorrhage [3]. Most maternal deaths are preventable through access to emergency obstetric care (EmOC) and evidence-based interventions such as active management of the third stage of labor (AMTSL). AMTSL includes administration of a pharmaceutical uterotonic (e.g. oxytocin or misoprostol) immediately following delivery to prevent postpartum hemorrhage (PPH) due to uterine atony [4,5].

As less than half of births in Sub-Saharan Africa are attended by a skilled provider, universal access to interventions such as AMTSL is low [6]. In this context, it is important for policies and programs to consider the widespread use of traditional medicines in the region during pregnancy and delivery. Hospital-based studies in South Africa have estimated that 43%–55% of women have used traditional preparations during pregnancy [7]. A South African study found that 32% of pregnant women utilized traditional preparations known as *imbelikisane* to induce or augment labor [8]. A recent Nigerian study found that 62% of surveyed women had utilized herbal medicines during pregnancy [9]. High proportions of traditional birth attendants (TBAs) provide herbal medications to women during pregnancy or at or near delivery, including for intended uterotonic effects [10–12]. Studies in Nigeria and Kenya documented that nearly 25% of TBAs utilized herbal preparations to expel retained placenta [13,14]. The Kenya study also noted that TBAs consider labor prolonged only after herbal medicines to augment labor have failed [14].

The fact that traditional medicines may have uterotonic effects is an important public health consideration [15]. A trial comparing a Tibetan traditional product with misoprostol for PPH prevention found that although misoprostol was more effective in reducing PPH, the traditional product had uterotonic effects [16]. While there may be potential for utilizing traditional preparations in PPH prevention, their uterotonic effects can also have adverse consequences, particularly if used to induce or accelerate labor. Studies in Malawi and Uganda have suggested that traditional medicines may be implicated in a substantial proportion of analyzed maternal deaths [17,18]. Other studies have suggested that herbal medicines are involved in adverse maternal and fetal outcomes such as uterine rupture and meconium aspiration [19–22].

A number of studies have investigated the pharmacologic activity of individual plants used at or near delivery. Resources such as the

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Prelude Medicinal Plants Database have documented the use of plants for numerous indications [23] and some reviews have documented plants used in traditional herbal mixtures taken during pregnancy and at or near delivery [24,25].

However, the literature is lacking a systematic investigation of traditional preparations used for intended uterotonic effects at or near time of delivery across Sub-Saharan Africa, as well as a systematic documentation of findings of pharmacologic investigations of preparations taken for these purposes. Finally, much relevant anthropological and ethnobotanical literature has not been organized and targeted for a public health audience.

2. Review objectives

The present structured review was undertaken with 2 objectives: (1) to describe the use of traditional preparations in Sub-Saharan Africa intended to have uterotonic effects at or near birth including inducing, augmenting, or speeding labor, or for preventing and treating PPH; and (2) to describe the results of pharmacologic investigations of uterotonic properties of traditional preparations used in Sub-Saharan Africa at or near time of delivery.

3. Materials and methods

A review of 13 medical, public health, and social sciences databases was conducted, restricted to periodical literature published between January 1, 1980 and June 30, 2010. Databases included Scopus, Global Health, Embase, JSTOR, CINAHL, PubMed, POPLINE, IndMED, CSA Sociological Abstracts, Anthropology Plus, AnthroSource, Development Experience Clearinghouse, and ProQuest Dissertations. The journal *Medical Anthropology* was also reviewed. Search terms combined words and phrases such as: home birth; traditional medicine; pregnancy; herbal; uterotonic; oxytocic; postpartum; hemorrhage; developing country; Africa; pregnancy outcome; labor (obstetric); and delivery (obstetric). Searches were adapted to databases' terminology and topic categories.

Journal articles identified through searches were included based on citation/abstract review if they were published in English within the specified period, contained primary data, and discussed use of traditional preparations in Sub-Saharan Africa. Articles were excluded based on citation/abstract review if they were review articles without primary data, referred solely to hospital practices, or exclusively addressed practices before 1980. Dissertations, conference publications, and books were excluded.

Articles meeting these criteria that could be located received full-text review. During full-text review, articles were excluded from analysis if exclusively describing:

- General classes of preparations (e.g. South Africa's *isihlambezo* and *imbelikisane*) without identification of specific plants.
- Use of traditional preparations early in pregnancy or in prenatal care, rather than at or near delivery.
- Use of traditional preparations for newborn care.
- Preparations that do not come into contact with the pregnant/delivering woman's body, e.g. "buried at door."
- Use of traditional preparations at or near delivery solely to prevent or manage infections or pain.
- Use of preparations to prevent or treat postpartum bleeding due to lacerations and other wounds (versus uterotonic mechanisms).
- Use of preparations derived from animal parts (few such preparations were identified, e.g. pangolin and sheep placenta).

For Objective 1, articles were also excluded if they were exclusively zoological or veterinary in focus, or described use of traditional preparations solely to prevent spontaneous abortion, induce abortion, or address menstrual disorders. For Objective 1 analysis, all plants with intended uterotonic effects were classified as used for one or more of the following indications: induce or augment labor; expel placenta or manage retained placenta; prevent or treat PPH; induce "oxytocic effect" without specification; induce another effect that may be uterotonic (e.g. "expel dead fetus"); and promote general maternal/fetal health.

Articles related to Objective 2 were excluded if they only conducted phytochemical or toxicity screening to identify constituents without testing of uterotonic activity. Articles related to Objective 2 were included even if their primary focus was preparations believed to have contraceptive or abortifacient effects, as long as uterotonic activity was evaluated. For Objective 2 analysis, 3 indication classifications were added: abortifacient, antifertility/contraceptive, and menstrual disorders. All included articles were abstracted using standard spreadsheet templates.

4. Results

4.1. Overview

Supplementary Material S1 (online only) provides a review flow diagram. Based on the search strategy, 12 076 non-duplicative references were identified. This large number resulted from using general search terms such as "traditional medicine" to ensure that relevant articles were not omitted. Inclusion and exclusion criteria were applied to these citations/abstracts leaving 271 references for full-text review. Of these, 187 met Objective 1 and 84 met Objective 2. If an article was included in the analysis following full-text review, inclusion and exclusion criteria were also applied to its bibliography, generating additional references for full-text review. Following full-text review of all relevant resources, 48 articles were included in Objective 1 analysis, and 54 articles were included in Objective 2 analysis. One study was included in both analyses because it gathered primary data regarding herbal agent use and conducted pharmacologic evaluations of identified plants [26]. Supplementary Material S2 (online only) lists all of the references included in the Objective 1 and Objective 2 analyses.

A number of articles with relevant content were not included owing to publication earlier than the inclusion period. The oldest identified resource documenting uterotonic effects of traditionally used plants was published in 1915, indicating that there has been awareness of the potential uterotonic activity of traditional medicines for much of the past century. Over 50 identified articles described use of traditional preparations during pregnancy in Sub-Saharan African countries (particularly Ghana and Nigeria) including for uterotonic purposes, but were excluded owing to absence of information about the specific plants utilized. Similarly, several studies were excluded because they documented the use of herbal mixtures (e.g. *sunungure* in Zimbabwe) to induce or augment labor without noting the specific plants used [27–29].

Many resources included in the analysis were published in journals from low-resource countries. This may partly be owing to the greater recognition of traditional medicine in these countries, including formal establishment of Centers for Traditional Medicine within Ministries of Health (e.g. in South Africa and Tanzania) as well as at the World Health Organization (e.g. The Collaborating Center for Traditional Medicine).

4.2. Objective 1 results

The 48 articles included in the Objective 1 analysis described usage of traditional uterotonics in 13 countries (Table 1). The most frequently studied countries were Tanzania (n = 12), Ethiopia (n = 9), and South Africa and Uganda (n = 7 each). Researchers interviewed traditional healers/herbalists (30 studies), general community members (12 studies), TBAs or other traditional midwives (10 studies), women (6 studies), and elders (4 studies). Sample sizes ranged from

Table 1
Objective 1: Studies documenting the use of traditional preparations for intended uterotonic effects.

Country (No. of studies)	First author	Year	Primary population (Sampled or described)
Cameroon (1)	Noumi E	2001	Community members, herbalists, traditional healers
Ethiopia (9)	Balemie K	2004	Traditional healers, elders
	Bekalo TH	2009	Male and female elders
	Giday M	2003	Elders (primarily male)
		2007	Traditional healers, farmers
		2009a	Male and female community members
		2009b	Male and female community members
	Jahn SAA	1991	Community members
	Lukelal E	2008	Knowledgeable individuals, traditional healers
	Wondimu T	2007	Community members
Gambia (1)	bij de Vaate	2002	Traditional birth attendants (TBAs)
Guinea (1)	Akendengue B	1992	Traditional healers
Kenya (3)	Morgan WTW	1981	Community members
	Nayningi MO	2008	Community members, traditional healers
	Voorhoeve AM	1982	Pregnant/recently delivered women
Malawi (1)	Bullough CHW	1982	TBAs
Nigeria (2)	Egwuatu VE	1986	Pregnant/delivering women, TBAs, traditional healers
	Irinoye OO,	2001	TBAs
Sierra Leone (1)	Lebbie AR	1995	Herbalists
Somalia (2)	Samuelsson G	1991	Traditional healers
		1992	Traditional healers
South Africa (7)	Arnold HJ	1984	Traditional healers
	Brindley M	1985	Elders (female)
	Jepson AP	1988	TBAs
	Selepe HL	2000	TBAs (including isangomas)
	Troskie TR	1997	Traditional healers/midwives, health providers
	van der Kooi R	2006	Pregnant women, health professionals, traditional healers
	Varga CA	1997	Women, traditional healers
Tanzania (12)	Chhabra SC	1987	Traditional healers
		1989	Traditional healers
		1990	Traditional healers
		1991	Traditional healers
		1993	Traditional healers
	Hedberg I	1982	Traditional healers
		1983a	Traditional healers
		1983b	Traditional healers
	Mahonge CPI	2006	Traditional midwives, traditional healers
	Maregesi SM	2007	Herbalists
	Mbura JS	1985	Antenatal care clients
	Ramathal DC	2001	Herbalists (among Rwandan and Burundian refugees)
Uganda (7)	Hamill FA	2000	Herbalists
		2003	Herbalists
	Kakudidi EK	2000	Community members
	Kamatenesi-Mugisha M	2007	Traditional healers/herbalists, TBAs, community members, women
	Oryem-Origa H	2003	Community members
	Ssegawa P	2007	Community members, traditional healers
	Tabuti JR	2003	Community members, traditional healers
Zimbabwe (1)	Tumwine JK	1991	TBAs

interviews with 7 TBAs [30] to a survey of 2200 recently-delivered women [31].

Included articles were published in public health, anthropological, and ethnobotanical journals. Public health articles often described traditional uterotonics in the context of efforts to train TBAs, understand TBA practices, or scale up use of skilled care at delivery. Some described traditional uterotonics in the context of research on presenting conditions at health facilities (including due to liver/kidney toxicity). Anthropological articles tended to discuss traditional uterotonics in the context of describing a particular culture's birth beliefs and customs or medical and religious practices. Ethnobotanical articles tended to mention traditional uterotonics in the context of documenting the traditional pharmacopeia across all medicinal purposes for specific tribes or in specific geographic areas (e.g. near parks or preserves), rather than targeting obstetric or reproductive indications. Owing to this variety of aims, included articles ranged from a study identifying 1 plant used to treat retained placenta out of 78 medicinal plants used by Kerreyua pastoralists in Ethiopia, to a study documenting 75 plants used to induce labor in just 2 districts of Uganda [32,33].

Interviews, guided field walks (including in ecologically fragile areas), or other systematic data collection approaches with traditional healers, elders, or men and women in communities of focus were used to identify plants. Descriptions of indications for use varied widely, and interview questions were not standardized across disciplines, countries, or investigation teams. As a result, stated indications required interpretation to determine whether they matched inclusion criteria. For example, the phrase “to ease delivery” might refer to pain relief and/or to accelerating labor. Many plants were perceived to have both uterotonic and non-uterotonic roles in labor and delivery (e.g. promoting good fetal or maternal outcomes).

The most common indications for use were to induce or augment labor, including in cases of prolonged labor or overdue pregnancy (185 plants). An additional 17 plants were described as being used for similar indications, such as to “relax” or “widen” the pelvis for delivery, or facilitate delivery. Sixty-one plants were described as being used to expel the placenta, shorten the third stage of labor, or manage retained placenta. Twenty plants were described as being used for PPH prevention or management, including indications such as “promoting tone” after delivery or “preventing

postpartum lesions." Eleven plants were described as being used for "general oxytocic effects" without specification, and 2 plants were described as used for other purposes that appear to be uterotonic (expel dead fetus and promote flow of lochia). The route of administration was primarily oral, with some topical administration and some venting of smoke/vapors into the vagina. Most oral preparations were infusions or decoctions, although in some cases the plant part (e.g. leaves) was eaten directly. The most commonly used plant parts were leaves, roots, bark and stems, and fruit.

Supplementary Material S3 Table 1 (online only) lists identified traditional preparations by species name and intended effects, and Supplementary Material S3 Table 2 (online only) provides additional information by each included study, including country of use, indications for traditional use, and routes of administration. A total of 208 plants were identified using primary data published between 1980 and 2010 as traditionally used for perceived uterotonic effect at or near delivery. An additional 19 plants were described by local or vernacular terms, without scientific names. Plants were generally identified in 1–2 studies; however, some plants were identified multiple times, with *Bidens pilosa* and *Cissampelos mucronata* identified most frequently (5 and 4 studies each). Several plants were used in multiple countries; for example, *Cissampelos mucronata* was identified in studies from 3 countries, but with varied indications for use. In Uganda, it was used for inducing labor and expelling the placenta, whereas in Ethiopia it was used for managing retained placenta. Similarly, in a 2007 study, Giday et al. [34] identified 4 plants traditionally used by the Shinasha, Agew-awi, and Amhara to manage bleeding after delivery, but no plants for other uterotonic indications. In 2009, the same lead researcher identified 6 plants traditionally used by the Meinit people to manage retained placenta, but no plants for other uterotonic indications [35]. It is unclear if these patterns are an artifact of data collection methodology or represent differences in cultural knowledge and perceptions regarding medicinal plants or the severity and amenability to treatment of different conditions.

Few papers included descriptions of pregnant women obtaining plants and compounding traditional medicines themselves. Very few articles provided information on dosage beyond frequency of administration.

4.3. Objective 2 results

The 54 articles included in the Objective 2 analysis described analysis of the uterotonic activity of plant species whose use was primarily described in 10 countries (with reference to additional use in Burundi, Congo, and Congo-Brazzaville). Table 2 summarizes the key evaluations conducted in each study. The most frequent focus countries were Nigeria (n = 22) and South Africa (n = 18); several studies also evaluated plants used in Ethiopia. As illustrated in Supplementary Material S3 Table 3 (online only), 81 plant species demonstrated uterotonic activity during in vitro pharmacologic evaluation. One study confirmed increase in in vivo oxytocin release following exposure to another plant extract (*Sida veronicaefolia*), but did not evaluate in vitro effects. One study confirmed uterotonic activity in a plant identified only by its local name.

Included articles evaluated between 1 and 70 plants for uterotonic activity. Articles were included in the Objective 2 analysis even if the studied plant's primary traditional use was as an abortifacient or antifertility agent, as long as uterotonic activity was assessed in a pharmacologic evaluation. The most frequent traditional uses of plants evaluated in studies included in the Objective 2 analysis were to induce/augment labor (n = 54), expel retained placenta (n = 18), and cause abortion (n = 14). A large number of plants were also used for antifertility purposes (n = 44), largely owing to inclusion of a study by Desta [36] of 70 plants traditionally used for this reason. Plants whose uterotonic activity was confirmed in 3 or more studies included: *Agapanthus africanus, Clivia miniata, Gunnera perpensa, Monechma ciliatum, Rhoicissus tridentata*, and *Spondias mombin.*

Studies varied widely in the details provided about experimental methodology (e.g. number of tissue samples, measures of contractile activity, dosages). However, in general, uterotonic activity was evaluated through in vitro experiments measuring effects of plant extracts and/or reference pharmaceutical drugs (e.g. acetylcholine) on isolated uterine tissue strips, generally from rats or guinea pigs. Most frequently, uterine strips were obtained from virgin rats or guinea pigs that had been administered stilbestrol or other estrogen 18–48 hours before being killed. Some investigations also used uterine tissue from gravid animals. Two studies evaluated the effect of pretreatment with the extract before the study animal was killed. Tissue strips were mounted in an aerated bath of Tyrode, de Jalon, or similar solution. Contractions were generally measured using force-displacement transducers and polygraph-type writing devices. Some studies used aqueous extracts to mimic traditional preparations, while others utilized alcohol extracts.

While all included articles evaluated changes in contractile activity, studies varied in defining such activity, choosing to focus on changes in frequency, amplitude, force, and/or tone, either in reference to spontaneous contractions or compared with a standard pharmaceutical drug's effects. Dose–response curves were generally constructed for each extract or drug tested.

As summarized in Table 2, 41 studies evaluated the potentiating or inhibitory effects of the extract when introduced in conjunction with other receptor-specific pharmaceutical agonists (e.g. acetylcholine) or antagonists (e.g. atropine). The most commonly proposed mechanisms of action for plants' in vitro uterotonic effects were mediation through cholinergic receptors, often muscarinic receptors, or promotion of prostaglandin synthesis. A number of studies simply characterized uterotonic activity as being similar or different in profile to oxytocin or ergometrine. In 19 studies, the ability of plant extracts to inhibit or potentiate contractile responses to pharmaceutical uterotonics was specifically evaluated, with potentiating effects on oxytocin responses frequently confirmed. Eighteen studies identified plant extract constituents (e.g. through phytochemical screening) and 6 conducted acute toxicity assessments (e.g. LD_{50} tests). For plants whose primary traditional use was as an abortifacient or contraceptive, studies also included evaluations of in vivo estrogenic/uterotrophic (n = 5), anti-implantation (n = 5), and/or abortifacient effects (n = 8).

Some studies identified variation in uterotonic activity within species, comparing extracts from plants harvested in different seasons, different parts of the same plant (e.g. roots versus seeds), or plants stored for different lengths of time (1 month versus 1 year). Katsoulis [37] and Katsoulis et al. [38] noted that few users or providers of traditional preparations appear to be aware of such variation.

5. Discussion

There is widespread use of traditional medicines at or near delivery in Sub-Saharan Africa. A wide variety of plants is used for perceived uterotonic effects, including to induce or augment labor, expel retained placenta, and manage postpartum bleeding. While some plants have been described as being used for uterotonic indications across borders, different regions and countries appear to have non-overlapping pharmacopeias. Many plants traditionally used to induce and augment labor demonstrate uterotonic activity during in vitro evaluations of their direct contractile effect.

Clinically, use of traditional uterotonic agents to augment labor may indicate an underlying labor disorder that is not amenable to herbal treatment. Additionally, uterotonic agents can lead to uterine hyperstimulation, fetal asphyxia, and other adverse outcomes [39]. Finally, as the use of pharmaceutical uterotonics during labor increases PPH risk, it is plausible that the more potent traditional preparations

Table 2
Objective 2: Studies conducting pharmacologic evaluation of traditional preparations.[a]

Primary country (No. of studies)	First author	Year	Evaluated effects on response to pharmaceutical uterotonics	Evaluated effects in presence of reference agonists and antagonists	Toxicity screening/ LD_{50} test	ID of constituents
Cameroon (2)	Frida L	2008	-	+[b]	+	-
	Kamanyi A	1992	-	+	-	-
Cote d'Ivoire (2)	Datte J	1996	-	+	-	-
	Zihiri GN	1996	-	+	-	-
Ethiopia (4)	Desta B	1994	-	-	-	-
	Gebrie E	2005	-	+	-	-
	Mekonnen Y	1999	-	+	-	-
	Tafesse G	2006	-	+	-	-
Ghana (1)	Lutterodt GD[c]	1995	-	-	-	-
Kenya (2)	Osore H	1982	-	+	-	-
	Sinei KA	1995	-	-	-	-
Malawi (1)	Bullough CHW	1982	-	-	-	-
Nigeria (22)	Aguwa CN	1987	-	+	+	+
	Akah PA	1994	+	-	+	+
	Bafor EE	2009a	+[d]	+	-	+
		2009b	-	-	-	-
		2010	-	+	-	-
	Falodun A	2006	+	+	-	+
	Ie O	2008	+	+	-	+
	Ladeji O	2005	+	+	-	+
	Nwodo OFC	1983	-	+	-	+[e]
		1988	-	+	-	-
		1991	+[f]	-	-	-
	Nworu CS	2007	+	+	+	+
	Oden Odu U	1995	-	-	-	-
	Offiah VN	1989	+	+	+	+
	Ojewole AJO	1982	-	+	-	-
	Okwusaba SC[g]	1997	+	+	-	-
	Onuaguluchi G	1999	-	+	-	-
	Owolabi OJ	2010	+	+	-	-
	Udoh FV	1999	+	-	+	+
	Uguru MO	1995	+	+	-	-
		1998	+[h]	+	-	-
		1999	-	-	-	+
South Africa (18)	Brookes KB	1999	-	+	-	+
		2006	-	+	-	+
		2007	-	+	-	+
	Kaido TL	1997	+	-	-	-[i]
	Katsoulis LC	1999	-	+	-	-
		2000	-	+	-	-
		2002	-	+	-	-
	Khan F	2004	-	+	-	+
	Mahomed IM	2006	+	+	-	-
	Mulholland DA	2002	-	+	-	+
	Sewram V	1998	-	+	-	-
		2000	-	+	-	+
		2001	-	+	-	+
	Veale DJH	1989	+	+	-	-
		1990	+	+	-	-
		1999	+	+	-	-
		2000	-[j]	+	-	-
		2001	-	-	-	-
Sudan (1)	Mohamed A-EH	1990	-	+	-	-[k]
Uganda (1)	Kamatenesi-Mugisha M	2007	+	-	-	-

[a] All articles included in the Objective 2 analysis documented that plant extracts produced some direct increase in contractile activity (e.g. increased frequency or amplitude of contractions), either in absolute terms or compared with reference pharmaceutical drugs.
[b] Evaluation of contractile activity in presence and absence of reference pharmaceutical noted, but results not explicitly described.
[c] This study evaluated the effect of the extract on in vivo oxytocin release.
[d] Refers to previous unpublished research documenting extract's inhibiting effect on oxytocin responses.
[e] Extracts partially analyzed for likely composition.
[f] Prostaglandin E2 administered in presence of plant extract and reference antagonist.
[g] In this study, the extract was administered to living rats, and uterine contractile activity in the presence of pharmaceutical uterotonics and other reference agonists/antagonists was evaluated in vitro after the animals were killed.
[h] Effects of oxytocin and other pharmaceutical uterotonics evaluated after in vivo pretreatment of study animals with plant extracts.
[i] Evaluation of concentrations of Na+, K+, and Ca++ extract solutions.
[j] Refers to previous studies evaluating potentiating effect of plant extracts on oxytocin.
[k] Fractions isolated, but constituents not identified.

may have a similar effect. A number of these plants also appear to potentiate the effects of pharmaceutical uterotonics and may have implications for dosing of oxytocin and other pharmaceuticals in clinical management.

However, the fact that some traditional preparations may be potent uterotonics also provides an opportunity for further research. Plant preparations may be useful in PPH prevention, particularly in settings where use of pharmaceutical uterotonics is not feasible. While there

appears to be variation in plant potency depending on preparation method, storage, and season, there is potential for national centers for study of traditional medicine to support development and standardization of effective, safe uterotonic products based on locally available plant materials. Additional research is needed to identify active agents in potent plants, determine mechanisms of action, and identify toxicities.

Three important implications for public health programs and research emerge from these findings. First, many plants traditionally used at or near the time of delivery have not yet been evaluated for uterotonic activity. The present review documents the use of traditional uterotonic agents in at least 19 countries, and over 270 plants with perceived or confirmed uterotonic effects. However, just 17 of these plants were discussed in studies included in both the Objective 1 and Objective 2 analyses. Uterotonic activity was confirmed in 82 plant species, but only a fraction of those identified as traditionally used for uterotonic indications. Additional research is needed regarding the uterotonic activity of plants traditionally used at or near the time of delivery and their mechanisms of action. The changing uterine sensitivity to oxytocin and other compounds later in pregnancy also necessitates study of potency on gravid uterine tissue as opposed to estrogen-primed tissue, which may manifest different responses to uterotonic compounds. It may also be useful to prioritize further in-depth research on the 6 plants whose uterotonic activity has been confirmed in multiple studies.

Second, much research on usage of traditional preparations for uterotonic indications was published during the 1980s and 1990s, when TBA training programs were widespread. Relatively few studies in the review were published in the last decade, during which TBA training has been discouraged by the international community [40]. Understanding current patterns of traditional uterotonic usage in light of increased access to pharmaceuticals for PPH prevention and treatment in Sub-Saharan Africa is also needed. Exposure to plants whose uterotonic activity is mediated through related mechanisms of action may interfere with or amplify the effects of these pharmaceuticals. Targeted research on traditional preparation use, including dosage and preparation practices, may be particularly important in Sub-Saharan African countries with high PPH-related mortality. With the more specific information now available on the uterotonic activity of herbal agents, investigations of near-miss and verbal autopsies on maternal mortality cases involving uterine rupture and stillbirth can be more complete. Similar research and investigations are needed in other settings where use of traditional medicines remains high and access to skilled care at delivery is low, such as parts of South Asia.

Finally, in settings where traditional preparations are commonly used for induction or augmentation of labor and have been shown to be potent uterotonics, this practice may be implicated in adverse outcomes such as uterine rupture and fetal asphyxiation. Maternal and newborn health programs may need to develop appropriate health education and behavior change messages to discourage such use. Formative research may be needed to identify the best way to develop and disseminate such messages. Given that induction and augmentation of labor are by far the most commonly cited uses for uterotonic preparations, there appears to be strong belief that traditional preparations are necessary to have appropriate labor or contractions. It is important to understand these beliefs to determine whether behavior modification (e.g. encouraging use of preparations only after delivery of the infant) can be promoted. Provider training may be needed to ensure that clinicians are aware of the local use of herbal uterotonics and obtain a history of such use from patients to inform clinical management decisions.

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Conflict of interest

The authors have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ijgo.2012.06.020.

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