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Review

Mechanism of retained placenta and its treatment by plant medicine in ruminant animals in Oromia, Ethiopia

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Retained placenta is the abnormal condition in animal reproduction in which fetal membrane failed to detach from maternal uterine wall after postpartum. The retention of placenta can create some disorders within reproductive organ of animals by allowing microorganisms to grow inside the uterus causing inflammation of uterus, fever, weight loss, decreasing milk yield, longer calving intervals and if the case is severe animals may die. The pathogenesis pathway of retained placenta development commences with an imbalance of antioxidant or oxidant capacity, decrease in estrogen production, decreased prostaglandin F2 alpha, and accumulation of arachidonic and linoleic acids in the placental tissue. Retained placenta can be treated with different methods such as manual removal, administration of intrauterine antibiotics, administration of hormonal therapy, and the use of plant medicine. The most common parts of plants used for drugs preparation are the leave, bark, root, stem and seed of the specific plant. The route of drug administration to animal is oral and vagina infusion. The herbal or plant prescriptions for treatment of placenta retention are characterized as antibiosis, antiphlogosis, immune enhancement and fertility improvement without endometrial injuries. The plants which have been used as treatment of retained placenta in Ethiopia are Flax seed, *Vernonia amygdalia*, *Dodonea angustifolia*, *Solanum acaule*, *Solanum acuminatum*, *Dovyalis* spp., *Galinsoga quadriradiata*, *Plumbago zeylanica*, *Momordica* spp., *Colocasia esculenta*, *Bryophyllum pinnatu* and *Urera hypselodendron.* The main objective of this paper is to illustrate the mechanism of retained placenta and its treatment using plant medicine in current status which helps the pastoral and clinician at remote areas and also to give enough information on the plant species that are sources of different chemical ingredient for future production of modern drug treatment for retained placenta.

Key words: Antibiosis, antiphlogosis, ethinoveterinarian, retained of placenta, treatment.

INTRODUCTION

Reproductive disorders are one of the major causes of decrease in reproductive efficiency and determinant of lifetime productivity of cows. The major causes of reproductive disorder in animals are abortion, dystocia, retained fetal membrane, pyometra, metritis, uterine and vaginal prolapsed, anoestrus and repeated breeding (Tagesu, 2018). Retention of placenta (ROP) is the abnormal condition in which fetal membrane failed to

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detach from maternal uterine wall after postpartum. It is also called retention of fetal membrane (RFM). Retention of placenta (ROP) occurs when fetal membrane fail to detach after postpartum within 8 h. Retention of fetal membranes from 6 to 24 h post parturition is termed retained placenta. It has been published in various journals in form of reviews and researches (Biner et al., 2015; Jemal, 2016; Swiefy, 2003; Tucho and Ahmed, 2017). It is better to illustrate the solution for retained placenta in developing countries. Ethinoveterinary have showed a great role in the treatment of animal diseases in developing country. Therefore, this paper stands to illustrate and coin out the problem, and solution to ROP in ruminant animals.

ROP can create some disorders within reproductive organ of animals by allowing microorganisms to grow inside the uterus thereby causing inflammation of uterus, fever, weight loss, decreasing milk yield, longer calving intervals and if the case is severe animals may die. Moreover, the animals which are in retained placenta can suffer from tetanus caused by tetanus organism which is commonly present in feaces and in the soil, and it requires at least 1 to 3 months as long term therapy. ROP can affect the economy of developing country, by decreasing economic growth rate mainly due to decreased milk yield and calf drop (Amin et al., 2013). Although the actual causes of retained placenta are not clear; the condition usually follows dystocia, maternal hypoimmunity, mal and unbalanced nutrition, stress, hereditary predispositions or infections (Hanafi et al., 2011).

PHYSIOLOGICAL ATTACHMENT AND DETACHMENT OF FETAL MEMBRANE

Cattle have cotyledonary placentas, wherein the fetal cot yledons are attached and envelop the maternal caruncles, forming the placentome. This connection is facilitated by villi from the cotyledons, and microvilli interactions at the cotyledon-caruncle interface. Collagen links the interface together at several sites, and the breakdown of this collagen is likely a key factor in placental separation (Eiler and Hopkins, 1993; Eiler and FECTEAU, 2007) (Figure 1).

The normal sequence of events initiating parturition involves fetal cortisol induction of placental enzymes that direct steroid synthesis away from progesterone and toward estrogen. Estrogen stimulates parturition by increasing the expression of the genes associated with myometrial excitability and contraction, and increases uterine sensitivity to oxytocin during the course of pregnancy. The increased estrogen can be up regulating the oxytocin receptors on the myometrium and secretion of prostaglandin F2 alpha (PGF2α). Therefore, oxytocin and prostaglandin produce strong contraction of uterine muscle (Fuchs et al., 2001).

Prostaglandin initiates myometrial contractions and results in lysis of the corpus luteum (CL).Lysis of the CL leads to secretion of relaxin and a further decline in progesterone. Both the secretion of relaxin and the decline of progesterone promote collagenase activity. Relaxin is well known for causing collagen lysis resulting in the softening of the cervix and relaxation of the pelvic ligaments. Thus, relaxin might also promote collagen breakdown at the fetal cotyledon-maternal caruncle interface. Conversely, progesterone promotes myometrial quiescence and suppresses collagenase activity. Thus, the decline in progesterone during the prepartum period could make allowances for the enzymatic activity necessary for placental separation (Fuchs et al., 1999; Maj and Kankofer, 1997). The mechanism of placental separation is detailed in Figure 2.

In the normal situation, serotonin plays a great role in the attachment of placenta. High fetal and placental serotonin during pregnancy could help to maintain placental attachment by promoting placental cell proliferation and inhibiting matrix metalloproteinase (MMP) activity (Fecteau and Eiler, 2001). The maturation of the fetal monamine oxidase enzyme system close to parturition could results in the metabolization and subsequent decrease in serotonin, which in turn could promote placental separation and parturition (Fecteau and Eiler, 2001). In addition to changes in the hormonal environment that favors the enzymatic breakdown of cotyledon-caruncle linkages, activation of the maternal immune response against the fetal membranes can play an important role in the breakdown of the placenta. Increased leukocyte chemotaxis and activity occur in cows with normally expelled placentas, and the cytokine interleukin-8 plays the role of a neutrophil chemoattractant in the cotyledon during parturition (Kimura et al., 2002).

The maternal immunological recognition of fetal MHC Class I proteins expressed by trophoblast cells triggers an inflammatory response that contributes to trophoplacental separation. These molecules, absent in early pregnancy, are expressed by fetal trophoblast cells in the 3rd trimester of pregnancy, and could play a role in initiating an inflammatory response that ultimately dissolves the adhesions between maternal and fetal portions of the placenta (Davies et al., 2000, 2004). Trophoblast secretes interferon-tau (IFN-τ) and both trophoblast and endometrium secrete prostaglandin E and the endometrial glands secrete serpins (uterine milk proteins), all of which inhibits lymphocyte activation to keep on the embryo not rejected by the dam (Hauguel-de Mouzon and Guerre-Millo, 2006). Class I MHC antigens expressed by trophoblasts prevent maternal NK-mediated cytotoxic responses (Entrican and Wheelhouse, 2006). Some researches propose that placental retention after normal parturition is more common when the presence of MHC Class I compatibility occurred between the dam and calves. This MHC Class I compatibility

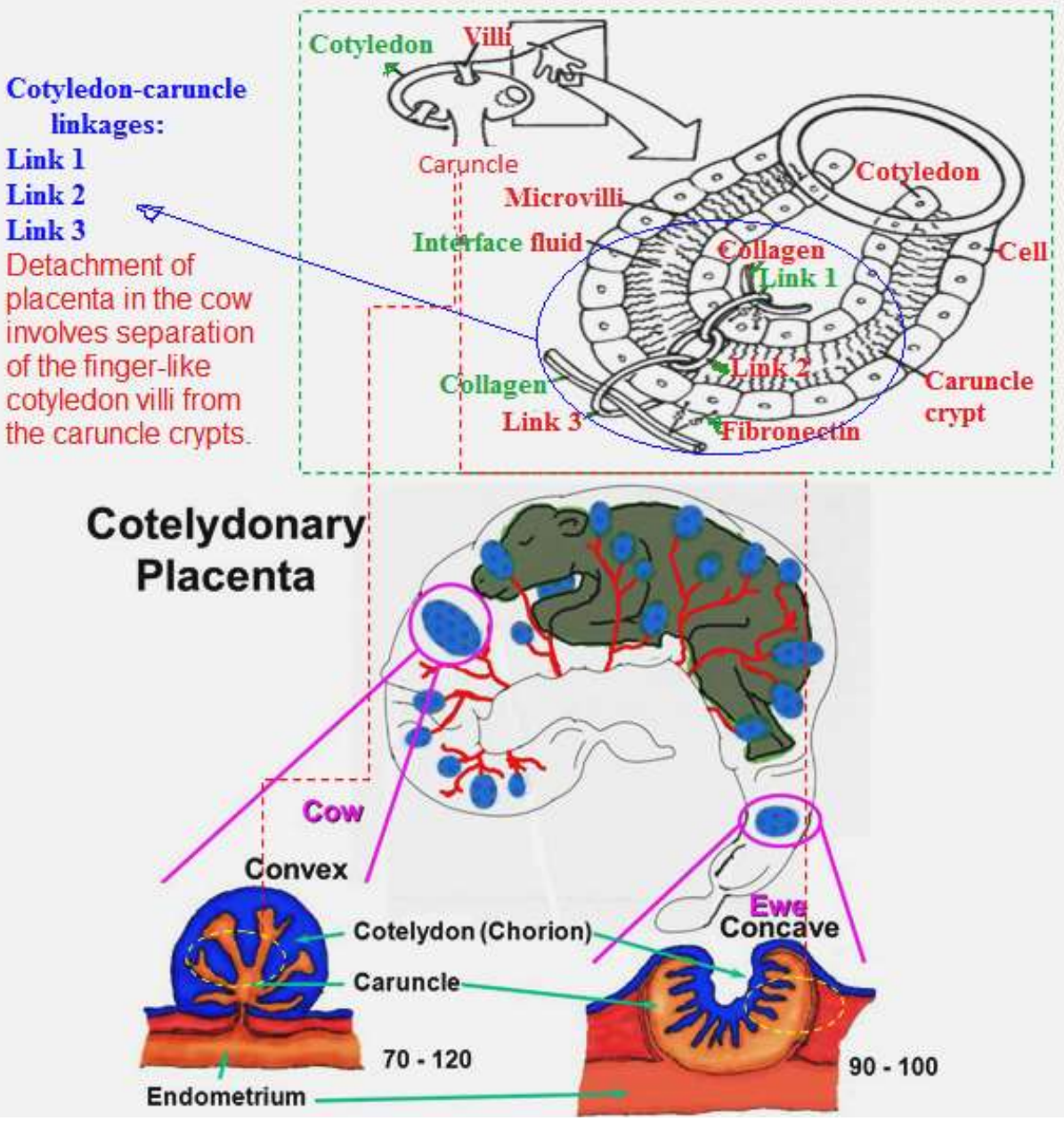

Figure 1. Structure of placenta and cotyledon- caruncle linkage.

implies genetic similarity in the MHC locus between fetus and dam which result in deficient alloreactivity of the maternal immune system against fetal antigens. All this leads to lack of cytokine production such as interlukin-2 and tumor necrotic factor alpha that are necessary for the maturation and shedding of placenta (Davies et al., 2004; Joosten and Hensen, 1992).

The increased cortisol concentrations in cows that developed retained placenta have immunosuppressive and inhibitory effects on leukocyte migratory activity (Engler et al., 2004). High progesterone and cortisol levels in the blood in stressed cows may induce accumulation of immunosuppressive proteins in the uterine lumen; this makes the uterus susceptible to infection and persistence of bacteria (Azawi et al., 2008; Kaczmarowski et al., 2006).

THE MECHANISM OF PLACENTA RETENTION IN RUMINANT ANIMALS

Pregnancy in dairy cows is considered to induce oxidative stress, which in turn can be a significant underlying factor to dysfunction host immunity and

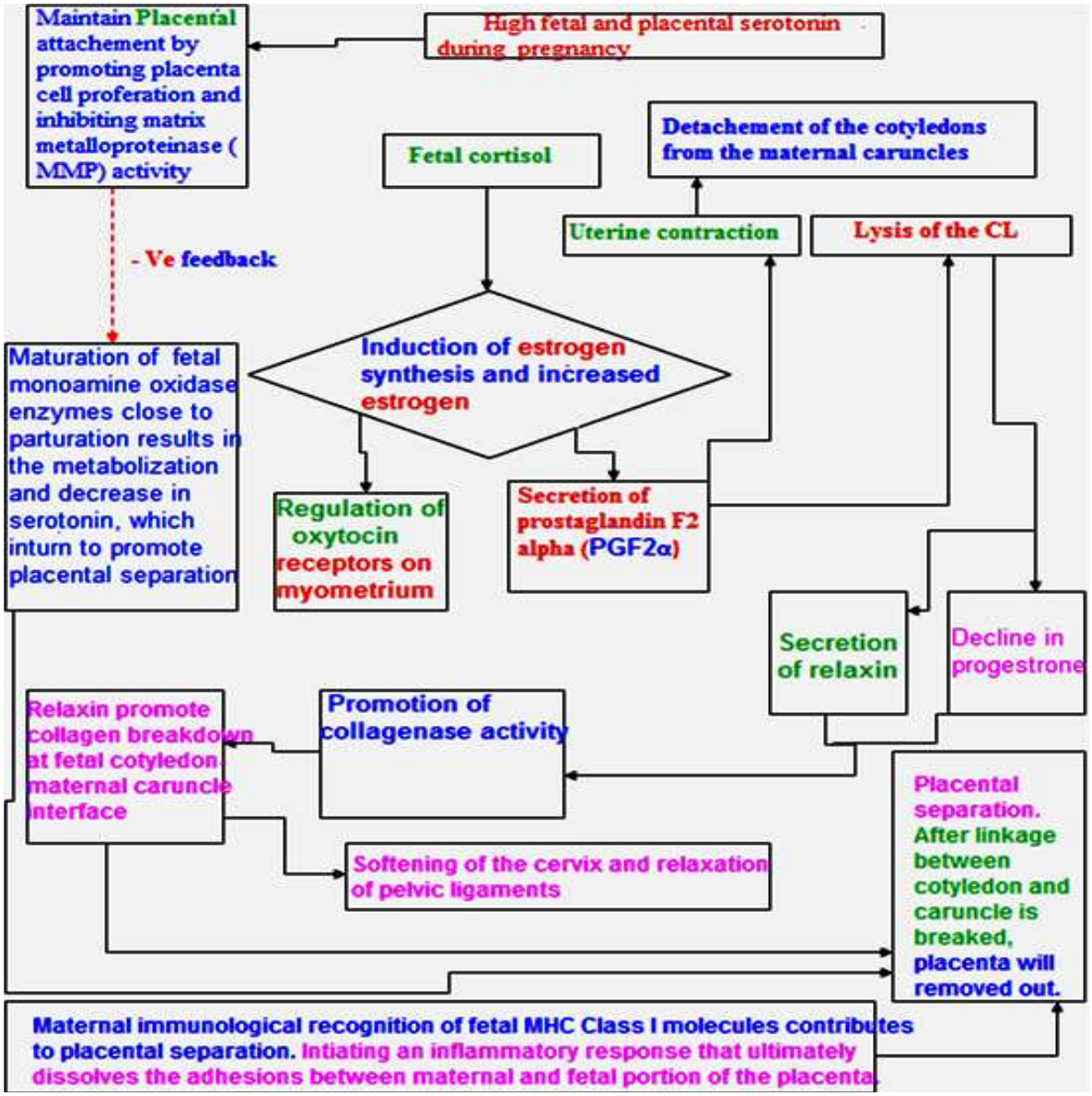

Figure 2. Mechanism of placental separation in domestic animals.

inflammatory responses and can increase the incidence of perinatal disorders (Sordillo and Aitken, 2009). The pathogenesis pathway of retained placenta development commences with an imbalance of antioxidant or oxidant capacity, decrease in estrogen production, decreased PGF2α and accumulation of arachidonic and linoleic acids in the placental tissue. Therefore, the diminishing effect of antioxidant can cause retained placenta in ruminant animals. It is necessary for the animal organism to maintain its antioxidative/oxidative process in the balance during prenatal period (Sordillo and Aitken, 2009; Wischral et al., 2001).

When the animals approach labor, hormone like prostaglandin and oxytocin are released, resulting in mechanical contraction of the uterus that is a vital role for normal delivery. The contraction persists into stages of labor and is responsible for expulsion of fetal membrane. However, when the contraction of uterus fails, the fetal membrane stays in uterus without expulsion. Therefore, the main case for retained placenta is the failure of uterine contraction which contributes to the detachment of cotyledons from maternal caruncles, and the lack of damage to fetal villi in normally expelled membrane which is not purely mechanical (Laven and Peters, 1996). Weakness of contraction of myometrium, lesion of cotyledon, edema of villus, heparin released by mast cells and the deficiency of trace minerals are involved in the retained placenta (Hehenberger et al., 2015). In

general, it is suggested that the placenta can be retained in uterus of animal due to lack of uterine contraction and inflammatory disorder which accumulate the arachidonic in placental tissue, also if the collagen which connects the caruncle to cotyledon is unable to breakdown; this causes the persistence attachment of fetal membrane in uterus of animals.

The events involved during detachment of fetal membrane or in cotyledon- caruncle detachment are listed as follows (Youngquist and Threlfall, 2006).

Morphological event

Detachment of placenta in the cow involves separation of the finger-like cotyledon villi from the caruncle crypts without significant tearing of either fetal or maternal epithelia. For the cotyledon villi to separate from the caruncle crypt, it is critical that the mouth of the cotyledon "pouch" be opened first by proteolytic enzymes. The separation of cotyledon from caruncle is achieved when the formation of the depression of the cotyledon toward the apex by digesting the edge of the cotyledon pouch occurred, then the finger-like cotyledon villi will be separated from the caruncle crypt.

After placental detachment is accomplished, uterine involution is completed in an average of 39 days in normal cows and 50 days in cows with retained placenta. By day 6 of postpartum, caruncle septa are disorganized; by day 15, caruncles are completely sloughed as a result of necrosis. Consequently, retained membranes are detached by caruncle necrosis within 6 to 10 days and not later than 17 days of post-partum. The surface of the endometrium is covered with new epithelium by day 26 to 30 post-partum (Youngquist and, Threlfall, 2006).

Biochemical events

The biochemistry of uterus after parturition is dominated by increased collagenase and protease activity that correlated with different stages of parturition, resulting in a massive breakdown of collagen and other proteins during uterine involution.

Physiological events

The physiological release of placenta is accomplished in most cows between 3 and 6 h postpartum. Cotyledon proteolysis (dehiscence) and decreasing adhesiveness (viscosity) of the cotyledon-caruncle interface fluids seem to be key factors in the release of placenta. Collagenases are capable of reducing the specific viscosity of collagen. Collagenase activity of cotyledon villi during delivery is increased in healthy cows and decreased in cows with placenta retention (Youngquist and Threlfall, 2006).

The cellular sources of collagenase and proteolytic enzymes for placental release in the cow are unknown. In laboratory animals and humans, myometrial cells, fibroblasts, and leukocytes have been identified as sources of collagenase in the uterus (Youngquist and Threlfall, 2006).

Lack of uterine motility is not considered as a reason for primary retention, since uterine motility is normal or above normal in cows with primary ROP. The direct cause of placental retention is uncertain, but it is related to a deficiency of myometrial contractions and failure of the maternal immune system to successfully degrade the placentomes at the end of pregnancy (Frazer, 2005).

The pathogenesis or development of retained placenta results from failure of timely breakdown of the cotyledon-caruncle attachments after delivering of the fetus (Figure 3). The most common causes for ROP are infectious and non-infectious diseases. Abortion, stillbirth, twinning, dystocia, induction of parturition with PGF2α, metabolic disorders like milk fevers and caesarian section, can cause retention of placenta (Frazer, 2005).

The spontaneous myometrial contractility is regulated by autocrine and paracrine release of PGF2α, the disturbance of endocrine function, high progesterone and cortisol levels, and low oestradiol level traced in the blood of cows with retained placenta (Kaczmarowski et al., 2006). Hormone imbalances existing before delivery are effective in inducing ROP. Increased progesterone level in ROP may be due to failure of the placenta to produce specific steroidal enzymes that help in progesterone aromatization and its conversion to estrogens (Ball and Peters, 2004).

Progesterone, more than estrogen, inhibits uterine collagenases and slows uterine involution. Dexamethasone increases synthesis and utilization of progesterone by cotyledon tissues in the cow. These changes may contribute to blocking postpartum expressio n of cotyledon collagenases. Moreover, it has been found that glucocorticoids down-regulate collagenases (Youngquist and Threlfall, 2006).

The large granulated binucleate cells in the trophectoderm of fetal membrane play a critical role in the parturition process. Binucleate cells produce placental lactogen and pregnancy associated glycoprotein (Ward et al., 2002). The increase in cortisol causes migration of binucleate cells from the fetal side of the placenta to the maternal side. When binucleate cell is migrated and becomes degranulated, there is increase in the concentration of placenta lactogen and other pregnant specific proteins (glycoprotein) (Drillich et al., 2006). These cells fuse with the endometrial epithelium and express MHC Class I on their surface. The villous portion of the placentome is the area of tight attachment and nutrient exchange. MHC Class I expression occurs prior to binucleate cell migration in this areas (Davies et al., 2000).

The cortisol on the fetal side which comes from the

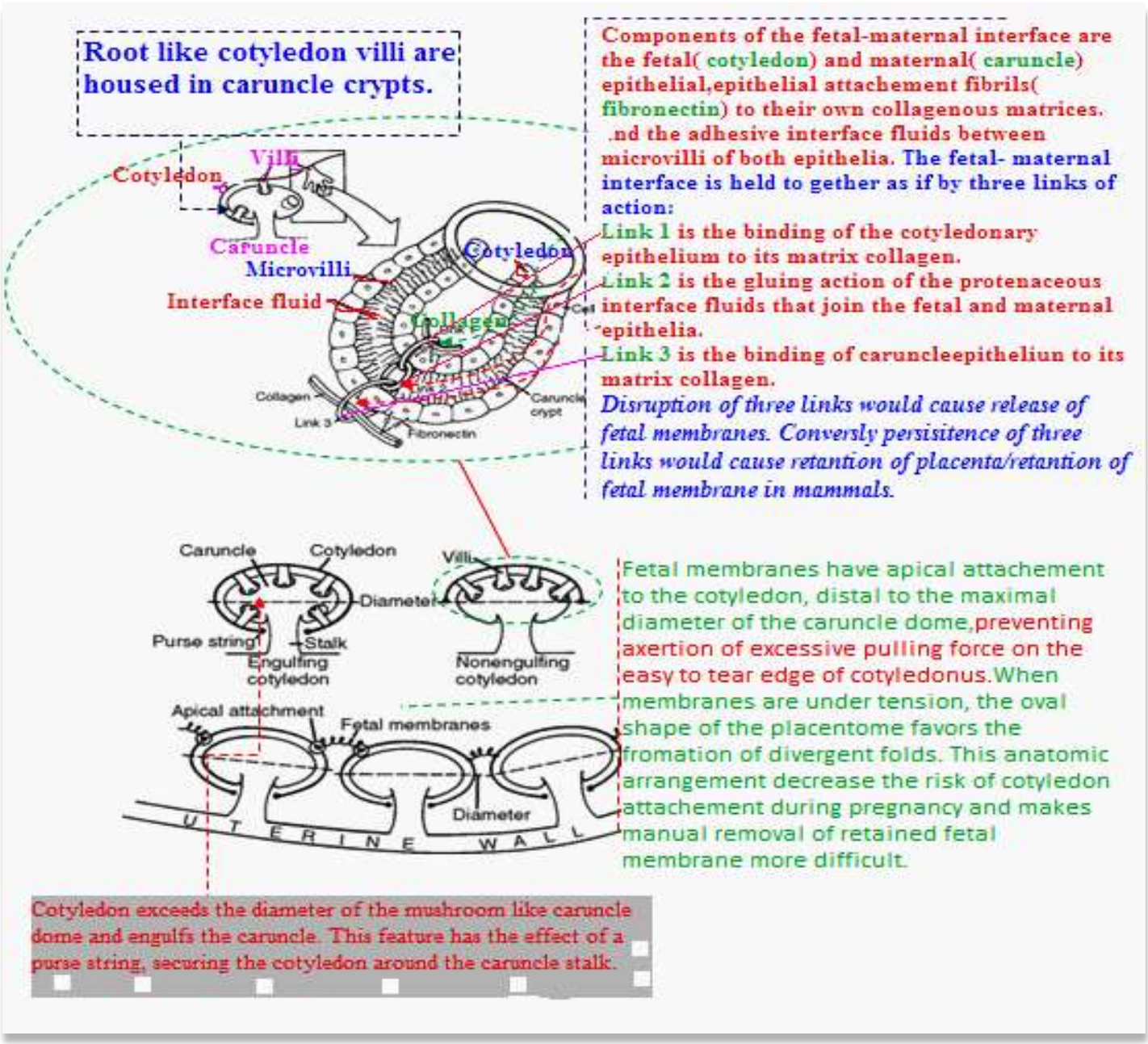

Figure 3. The components of caruncle- cotyledon linkage and mechanism of retained placenta.

fetal adrenal gland is the first critical initiation of placental separation or detachment. The fetal adrenal gland is stimulated by adrenocorticotropic hormone due to maturation of the fetal hypothalamus and stress axis near the time of expected parturition. The fetal cortisol can reach a critical level of about 30 h prior to normal parturition; the increasing cortisol concentration is only on the fetal side of the circulation. Any increase in circulating cortisol in the maternal circulation is due to production of cortisol by the dam adrenal gland (Ward et al., 2002).

TREATMENT FOR RETAINED PLACENTA IN RUMINANTS

General fact for treatment of retained placenta in ruminant animals

The treatment of ROP is carried out by detachment of the membrane in order to avoid or reduce the inflammation and other disease, decrease milk losses, and reduce reproductive inefficiency. The therapy treatment of

retained fetal membrane is a controversial subject. Intrauterine antibiotics are routinely administered, although their effect on fertility parameters is under question (Biner et al., 2015). Retained placenta can be treated using different methods such as manual removal, administration of intrauterine antibiotics, administration of hormonal therapy, and the use of plant medicine (Ethinoveterinary methods).

The manual removal of the placenta remains a common practice in every veterinary clinic, despite many studies had failed to demonstrate its benefit on reproductive performance. A study revealed that comparing manual removal and intrauterine antibiotic therapy along systemic treatment of febrile cows found no difference in reproductive outcomes, when compared with the use of systemic therapy of the febrile cows alone (Drillich et al., 2006, 2007).

Manual removal can result in a more frequent and severe uterine infections. More conservative treatment and manual removal prolonged the interval from calving to1st functioning CL by 20 days. Removal of an attached placenta can cause damage to the endometrium and suppresses uterine leukocyte phagocytosis, both of which encourage bacterial invasion and they all have effect on fertility of animals (Drillich et al., 2007; Eiler and Hopkins, 1992). Tetracycline antibiotics commonly used for intrauterine treatment in cattle inhibits matrix metalloproteinase (MMPs) and interferes with the normal placental detachment mechanisms. The breakdown of collagens plays a role in placental detachment and infusion of collagenase which can be helpful in breaking the caruncle- cotyledon bond in retained fetal membrane. Injection of 1 L saline containing 200,000 IU of bacterial collagenase into the umbilical arteries of retained placentas caused earlier placental release than untreated contemporaries (Sheldon et al., 2006).

If applied within 24 to 72 h after calving, collagenase treatment can cause release of membranes in cows within 36 h. This treatment is targeted specifically at correcting the lack of cotyledon proteolysis and might be more effective than traditional therapies (Eiler and Hopkins, 1992). In general, manual removal and giving of intrauterine antimicrobial have been practiced to treat retained placenta (Sheldon et al., 2006).

Vitamin supplementation like antioxidants, vitamin E and selenium by single IM injection at week 3 prepartum is used as prophylactic dose to avoid placental retention in cows. The hormonal treatment of ROP is done by administration of prostaglandin, oxytocin and other steroidal hormones. PGF2α does not cause detachment of retained membranes, but it can improve reproductive performance in the early postpartum cow due to the uterokinetic effect (Gupta et al., 2005; Hauguel-de Mouzon and Guerre-Millo, 2006). Glucocorticoids (dexamethasone) could have a direct inhibition effect on collagenase activity which inhibits PGF2α synthesis within cotyledon cells (Gupta et al., 2005).

Oxytocin is the best hormonal choice for treatment of retained placenta in the early postpartum in animals. 20 IU three to four times daily have been used for retention of placenta, which acts as uterokinetic (Youngquist and Threlfall, 2006). Antimicrobial agent is also important in such treatment and it can treat secondary bacterial infection as well. The antibiotic required in the treatment of ROP are called intrauterine antimicrobial like tetracycline (powder 5 g) and procaine penicillin G intramuscular (IM) on day 1 to 3 which is used in endometritis (Youngquist and Threlfall, 2006). The treatment of retained placenta has been carried out by many clinicians and veterinarians; they used different methods such as manual removal, hormonal and non-hormonal like intrauterine antimicrobial and the like. This paper stands to illustrate the best treatment for ROP in remote areas; places where there are no clinics or drugs available, the drug for treatment of retained placenta is prepared from natural plant species.

Plant source of medicine used for treatment of retained placenta in ruminants

Plants are sources of various chemicals and secondary metabolites which have medical value in human and animal health. In the traditional way, the farmers treat their animals by administration of plant extract juice in patient animals. The herbal or plant prescriptions for treatment of retention of placenta are characterized as antibiosis, antiphlogosis and immune enhancement and fertility improvement without endometrial injuries. The survey data collections were conducted in Oromia region. The following plants have been used for treatment of ROP in Ethiopia: Flax seed (*Ija talbaa*), *Vernonia amygdalia* (Eebicha), *Dodonea angustifolia* (Itacha/Hitacha), *Ensete ventricosumis*(Warqee), *Grewa ferrugina*, *Solanum acaule* (Iddii hoolaa), *Solanum acuminatum*(Iddii saree), *Dovyalis* spp. (Koshommii), *Galinsoga quadriradiata* (Waasee), *Plumbago zeylanica, Momordica* spp. (Qorii simbiraa), *Colocasia esculenta* (Goodarree), *Bryophyllum pinnatu* (Bosoqqee) and *Urera hypselodendron* (Laanqessaa) summarized in Table 1. These plants are sources of secondary chemical metabolites which act as antioxidant, antimicrobial and anti-inflammatory used to relief animal from pain and removal of placenta. In Ethiopia, especially in Oromia region, plants part like roots, leaves, stems, barks and seeds are collected and dried in order to prepare the extraction of chemical in form of powder and juice. The collected plants are used for treatment of ROP with a combination of other plants in order to increase the effectiveness of chemical. The combination of two different plants extract is better than extract chemical from a single plant. The following plants are common in the treatment of ROP. The preparation methods are like the root of *Momordica* spp. (*Qorii simbiraa*) which is

Table 1. The common plants used for treatment of retained placenta in Ethiopia, Oromia.

Local name (AfaanOromoo)	Scientific name	*Family name*	Part of plant	Use and route of administration
Leemmana	*Bambusa vulgaris*	*Poaceae*	Leaf	The feeding leaves of *Bambusa vulgaris* mixed with *Qunda barbaree* helps in expulsion of placenta. The leaves is dried and mixed with water, given to cattle orally (http://www.hillagric.ac.in)
Eebicha	*Vernonia amygdalia*	*Asteraceae*	leaf	Leaves of *Vernoniaamygdalia* used treat ROP by mixing with table salt, and then administer to cow orally (Yigezu et al., 2014)
Talbaa	*Linum usitatissimum*	*Linaceae*	Seed	The powder of flax seed is mixed with water or salt, and then given to animals orally
Kosorruu adii	*Argemone mexicana*	*Papaveraceae*	Root	The powdered part is mixed with water, then administer to animals (Yadav et al., 2014)
Adamii (isabattee)	*Opuntieficus indica*	*Cactaceae*	leaf	Chopping the leaves and mixing with water and administering to animal orallywith balanced dose (Bobaso, 2016).
Itacha/Hitacha	*Dodonea angustifolia*	*Sapindaceae*	leaf	The leaves is powdered and administer to animals orally, the chemical extraction increases the contraction of uterus which facilitates the expulsion of placenta (Tekle, 2014)
Warqee (Enset, kocho)	*Ensete ventricosum*	*Musaceae*	Leaves	Leaf of *Ens*et is given for animals, and then the animal may relief from ROP (Mekonnen et al., 2016).
Qobboo	*Ricinus communis*	*Euphorbiaceae*	Leaves, seed	The dried part of the *Ricinus communis* is mixed with water and given for cow to repulsion of placenta (Birhanu et al., 2015).
Koshommii	*Dovyalis* spp.	*Flacuourtiaceae*	Leaf	Leaf of *Dovyalis* is chopped and mixed with hot water and given for animal orally (Tolossa et al., 2013)
Qorii simbiraa	*Momordica* spp.	*Cucurbitaceae*		The root of *Momordica* spp is collected, dried ground and mixed with the powdered root of *Colocasia esculenta, then this mixed powder is soaked in warm water and one cupful filtrate drenched into animals (*Tolossa et al., 2013*)*
Bosoqqee	*Bryophyllumpinnatu*	*Crassulaceae*	Leaf	The latex part of leave or stem is mixed with *Urera hypselodendron* (*Laanqessaa)* collected and applied into intrauterine of cow (Tekle, 2014).

collected, dried, ground and mixed with the powdered root of *Colocasia esculenta,* and then this mixed powder is soaked in warm water and one cupful filtrate drenched into animals. After 24 to 48 h, the placenta would be ejected from the suffered animal. *Dovyalis*spp (*Koshommii*) is used to remove retained placenta, the leaf will be chopped and mixed with hot water and given to the animal orally (Tolossa et al., 2013).

In rural areas where modern medicine is inaccessible to farmers, Ethnoveterinary medicine (EVM) is often used to expel retained placenta in livestock. Ethnoveterinary medicine is a scientific term for traditional animal health care that encompasses the knowledge, skills, methods, practices, and beliefs about animal health care found among community members (McCorke, 1986).

Ethnoveterinary medicine is the community based local knowledge and methods in caring, healing and management of livestock in remote area where modern medicine is limited, and it has been developed through some trial and errors, and experiments (Misra and Kumar, 2004). Ethnoveterinary medicine is sustainable and ecologically sound because plant products with recognized medicinal properties are far more accessible to the villagers than Western medicine. The EVM is a cheap and easy accessible alternative to expensive pharmaceuticals, this help the farmer make it available

at low cost or no cost at all (McGaw and Eloff, 2008).

The traditional remedies which have been used in treatment of retained placenta throughout the world are like salty water, soap detergent solution, *Terminalia serecea* roots, *Spirostachys africanum* bark and *Burkeaa fricanum* bark. Other herbal plants included *Ziziphus mucronata, Peltophorum africanum, Elephantorrhiza elephantina, Pouzolzia mixta, Dicerocaryu meriocarpum, Asparagaus* spp., *Hermaniaguerkeana, Ozoroapaniculosa, Scacdoxus* spp. and *Boscia albitrunca* (Moreki et al., 2012).The remedies are administered either as a decoction or infusion. In the present study, the common plant parts used for treatment of retained placenta are barks, roots and bulbs and parts and products of animals such as skins and hides, bones, milk, butter and even urine and dung, are ingredients of Ethinoveterinary medicine (Balaji and Chakravarthi, 2010).

Methods of preparation and administration of medical plant for animals

The preparations of these plants are, first collection of the leaves, roots and barks of the plant, then extraction of chemical in form of juice and powder, after which they are mixed with each other. After the plant extraction is prepared, the extraction is administered into the animals orally or through vaginal application of animals; this is done to detach the fetal membrane from its attachment. As the data were collected from community, they are informed that the methods of drug preparation from plants are concluded as follow; first the collection and identification of the plant, then drying the plant part like leaf, stem and root by putting it under shade and making it into powder. Afterward it is mixed with water and if available with salt water, then administered to animals through oral and intrauterine. The retained placenta would be removed from animal after 2 to 3 days. The most common plant which have been in use in Oromia region is flax seed (*Linum usitatissimum*).This flax seed is first grinded to form powder, then mixed with water and if available salt water(Na cl).After everything is prepared from powder of flax seed directly administering into animal orally. After one day the placenta will be removed from dairy cow and ewes. The common plant parts which are used in preparation of drug are leaves, stems, seeds, roots, barks and cell wall combs.

The most common plant used for treatment of retained placenta in Ethiopia

Dodonaea viscosa

The origin of *Dodonaea viscosa* is believed to be Australia, but, currently it is distributed in the tropics and subtropics part of the world. The plant *Dodonaea viscosa (D. vincosa*) is distributed to Africa (Ethiopia and others), Asia, Australasia, North America, and South America (Rani et al., 2009).D. viscosa is a shrub that grows to 3 meters tall and is indigenous in most Ethiopia regions like Oromia. Ethnopharmacology reporting in different parts of the world indicates a variety of therapeutic uses. The extracts leaves of this plant exhibited antibacterial and antioxidant properties (Riaz et al., 2012; Teffo et al., 2010).

D. vincosa acts as an antioxidant, antimicrobial, anti-inflammatory, induce wound healing and antispasmodic effect (Riaz et al., 2012; Teffo et al., 2010; Khan et al., 2012; Salinas-Sánchez et al., 2012. The chemical extract (alkaloids, tannins,phenols,gums and mucilage, fixed oils and fats, saponins, proteins, volatile oils,flavonoids and steroids) from *D. vincosa* by ethanolic extract, n-hexane, dichloromethane, ethylacetate, n-butanol, Chloroform, Ethanol and methanol crude extract from stem, bark and leaves act as antimicrobial. Gram positive bacteria were more sensitive to the extract of *D. vincosa* than Gram negative bacterium (Khurram et al., 2009 Ansar et al., 2013). Chopped leaves of *Dodonea angustifolia/ (Hittacha in AfaanOromo)* mixed with water are filtered for treatment of retained fetal membrane (Tekle, 2014).

The plant contains many flavonoids: alizarin (5,7,4’-trihyd roxy-3’-(3hydroxymethylbutanol) 3,6-dimethoxy flavone), pinocembrin (5,7-dihydroxy flavanone), penduletin,(5,4-’ Dihydroxy3,6,7-trimethoxy flavone); isokaempferide (3,5, 7,4’-tetrahydroxyl-3’-methoxy flavone). 5,7-dihydroxy-3'-(4''-acetoxy-3''-methylbutyl)-3,6,4'-trimethoxy flavones; Kaempferol methyl ethers, 3, 5, 7-trihydroxy-4'-methoxyflavone ; 5, 7, 4'-trihydroxy-3, 6-dimethoxyflavone; 5, 7-dihydroxy-3, 6, 4'-trimethoxyflavone (santin); 5-hydroxy -3, 7, 4'-trimethoxyflavone; 3,4',5,7-tetrahydroxy flavones (kaempferol). 5,7,4'-trihydroxy-3',5'-di(3-methylbut-2-enyl)- 3,6-dimethoxyflavone and 5,7,4'-trihydroxy-3'-(4-hydroxy-3-methylbutyl)-5'-(3-methylbut-2-enyl)-3,6-Dimethoxyflavone;acacetin-7-Me ethers the flavonol-3-methyl ethers 4',5,7-trihydroxy-3,6-dimethoxyflavone, penduletin; 3, 6, 4'-trimethoxy-5,7-dioxyflavone; kaempferol 3,7-di-methyl ether and kaempferol-3,4',7-trimethyl ether were isolated from the aerial parts. Isorhamnetin and quercetin were isolated from the root bark of *D. viscosa.* Catechin or chromene groups, chalcones with trimethoxyphenyl group and tannin with 4-O-β-D-xylopyranoside were isolated from the leaves of *D. viscosa* (Abdel-Mogib et al., 2001; Muhammad et al., 2012; Niu et al., 2010 ; Teffo et al., 2010; Zhang et al., 2012). The chemical extraction mentioned above act as antioxidant and activation estrogen production. The chemical extraction also increases the contraction of uterus which facilitates the expulsion of placenta. The mode of action of *D. viscosa* extraction does not only act as antioxidant and muscle extraction, but also act as antimicrobial and antinflamatory which prevent shock and systemic disease from animals.

Vernonia amygdalia

Vernonia amygdalia, member of Asteraceae family, is a small shrub that grows in tropical Africa. *V. amygdalia* is a rapid regenerating soft wooded shrub of 2 to 10 m tall with petiolate leaves of around 6 mm in diameter. *V. amygdalia* is valuable medical plant that is distributed throughout Africa (Ijeh and Ejike, 2011; Yeap et al., 2010). It is used as active anti-cancer, antibacterial, antimalarial and antiparasitic agent (Clement et al., 2014; Yeap et al., 2010). As one study revealed, the leaf extracts of *V. amygdalia* have hypoglycaemic and hypolipidaemic properties in experimental animals and is used in managing diabetes mellitus (Iwara et al., 2015).

The common name of this plant varies in ethnic groups around world. In Ethiopia it is termed as '*Eebicha*' in *Afaan Oromo*, in *Amharic* it is termed as '*Grawa'*. The methods of chemical extraction from leaves, stem and bark of *V. amygdalia* has been reported in many researches. In the traditional way, the community prepares the extraction by grinding and filtering the leaves of the plant.

First step is collection of the plant parts, then keeping it dry and after that, they make powder and mix with water, filtering with some filter paper or piece of cloth and administering to the animals. In the modern ways, first collection of the plant is submitted to the laboratory and the chemical is extracted using different procedure of chemical extraction (Odey *et al*., 2012).

The leaves of *V. amygdalia* has been used to treat retained placenta by mixing with table salt, then administered to cow orally, and after some time the animal is relieved from retained placenta(Birhanu and Abera, 2015; Tekle, 2014). The ethanolic leave extract of V. amygdalia have secondary metabolity chemical which acts as antimicrobial such as terpenes, oxalate, coumarins, lignins, sesquiterpenes, phytate, tannins, saponins, flavonoid, cyanogenic glycoside, alkaloids, anthraquinon,steroid and phenol (Owoeye et al.,2010; Udochukwu et al., 2015).The antioxidant, antimicrobial, anti inflamatory, antiseptic and disinfectant, antifungal, anticancer and antifouling effect of the chemical extracted from *V. amygdalia* is used to relief the animals from retained placenta and other complicated dis eases (Igwe et al., 2015).

Phenol 3, 5-bis (1, 1 dimethylethyl), palmitic acid (Hex adecanoic acid), 1, 2-benzenedicarboxylic acid, Di-n-octyl phthalate, 9, 12-octadecadienoic acid (linoleic acid) and oleic acid

Flavonoids present in *V. amygdalia* are like luteolinluteolin 7-0- beta-glucuronoside and luteolin 7-0-beta-glucoside; these possess antioxidant activity (Audu et al., 2012; Yeap et al., 2010). Therefore this paper stand to illustrate the effect of *V. amygdalia* in treatment of retained placenta after postpartum by acting on the prevention of microorganism growth and as antioxidant. The action of chemical extract from *V. amygdalia* act as increasing uterine contraction by decreasing progesterone concentration, this increment of uterine contraction may enhance removal of retained placenta (Yeap et al., 2010; Kamatenesi-Mugisha, 2004).

There are so many plants which are important in the treatment of retained placenta in domestic animals and even in human beings. The chemical which extract from those plants act as antioxidant, antimicrobial and initiates the contractility of the uterus, thus placenta are easily detached and removed out of the uterus. It is suggested that the tannin produced from the plant act as astringent to facilitate the contractility of uterus and removal of placenta.

When the wall of the uterus undergoes contraction, there may be shrinkage of small blood vessels and villi and the fetal caruncle easily detached from cotyledon of maternal, as a result, expulsion of placenta may occurred. Tannins containing plants are effective where protection of underlying tissues by skin or mucosa is compromised as seen in the case of wounds and retained placenta. Tannins proteins complexion limits fluid loss and forms a physical barriers to further tissue insult (Bruneton, 1995). Astringent property of tannins has a physiological effect such as contraction of the uterus which might facilitate the removal of retained placenta. By shrinking of the small blood vessels, the capillary pressure is lessened and separation of fetal membranes occur (Bruneton, 1995; Manspeaker, 2007). *Ricinus communis* has been used to treat retained fetal membrane (Birhanu and Abera, 2015). In treating retained fetal membrane, the leaf of *Ensete ventricosum i*s also given for cow (Mesfin et al., 2016).

The plant extract of *Grewia ferrugina were* useful for easy expulsion of placental membranes. The feeding of bamboo leaves (*Bambusa vulgaris*) mixed with black pepper (*Qunda barbaree*) helps in expulsion of placenta. Raspberry leaves when fed to pregnant mares during the last 45 days of gestation reduce the incidence of peri-parturient diseases viz prolonged labor, retained placenta (www.hillagric.ac.in). *Argemone Mexicana (*Kossorruuadii) is used to remove retained placenta. 100 g whole Argemone mexicana plant with any available local grass for feeding once a day is used for removal of retained placenta in cows (Yadav et al., 2014).

Opuntieficus indica (Adamii ishee battee) and *Urera hypselodendron* is used for expulsion of placenta retention by chopping the leaves and mixing with water and administering to the animal orally (Bobaso, 2016; Tekle, 2014). The chemical extraction is being performed in laboratory by different methods. However the modern extractions of chemical from plant parts are not known at the remote area where modern laboratory is scant. The farmers were used to administer the traditional medicine

without any extraction, this paper stand to report how to treat the retained placenta and identification of which species of plant are used for treatment of retained placenta in Ethiopia. Generally in Ethiopia, so many medical plant species exist. Out of these plants, the most common medical plants are rich in secondary chemical metabolites, which act as antimicrobial, antiparasitic, antispasmodic, analgesic, anti-cancer and anti-fungal and etc. The discussed plants are not published in any journal, this paper is pioneer to this study, and the most common way in treatment of ROP by chemical extraction is from the mixed chemical of different plant in order to increase the broad spectrum effect of drug.

The broad spectrum effect of this extracted drug acts a s antiflamatory, antispasmodic, antioxidant and antimicrobial. The extraction from the mentioned plants also used in enhancing the production of estrogen, and increasing contraction of uterus which facilitate removal of retained fetal membrane. Actually, the community used to treat their animals by separating plant extraction, and mixing the extracted chemical with other different chemicals.

All plants are effective, but drug is more effective when extractions of different plants are mixed rather than single plant. The orally drenched is more effective than others, because the toxicity of this extracted chemical is biotransformed and absorbs into the system, thus it easily reaches the uterus wall. The intrauterine application is also effective, however it is not practiced much in community. Moreover, the intrauterine infusion of this extracted drug from the mentioned plants may causes some disorder, and the toxicity of that chemical may have effect on the fertility of animals. Therefore, from this research it can be said that the orally drenched of extracted chemical from Ethinoveterinary medicinal plant is better than intrauterine infusion in the treatment of ROP.

Conclusion

Retained placenta is common in domestic animals like ruminants and equines. The most common causes of ROP are dystocia, caesarian section, maternal hypoimmunity, mal and unbalanced nutrition, stress, hereditary predispositions or infections, failure of uterine contraction. Retention of placenta in ruminant animals have negative influence on the economic development of developing country by decreasing milk production, the inflammation of uterus, fever, weight loss, longer calving intervals and dying of animals. The treatments for retained placenta have been operated by different methods like hormonal and non-hormonal methods. The plant medicine which is used for treatment of retained placenta in ruminant animals are listed as follow: *Terminalia serecea* roots, *Spirostachys africanum* bark and *Burkeaa fricanum* bark. *Ziziphus mucronata*, *Peltophorum africanum*, *Elephantorrhiza elephantina*, *Pouzolzia mixta*, *Dicerocaryu meriocarpum*, *Asparagaus* spp., *Hermania guerkeana*, *Ozoroa paniculosa*, *Scacdoxus* spp., *Boscia albitrunca*, *Vernonia amygdalia* (Eebicha*), Dodonea angustifolia* (Itacha/Hitacha), *Ensete ventricosumis*, *Grewa ferrugina*, *Solanum acaule* (Iddii hoolaa), *Solanum acuminatum* (Iddii saree), *Dovyalis* spp. (Koshommii), *Galinsoga quadriradiata*, *Plumbago zeylanica*, *Momordica* spp. (Qorii simbiraa), *Colocasia esculenta* (Goodarree), *Bryophyllum pinnatum* (Bosoqqee), *Linum usitatissimum* seed (IjaTalbaa) and *Urera hypselodendron* (Laanqessaa*).* The effects of retained placenta in domestic animals are critical in increasing mortality rate and decrease of economy in developing country. Therefore, this paper leads and gives the solution for the treatment of ROP in developing countries or remote areas where modern medicine is not available and veterinary clinic is scant. This paper also tends to apply some concept and information for production of drug from the mentioned plants in future industry.

CONFLICT OF INTERESTS

The author has not declared any conflict of interests.

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